Impact of sodium and ultrafiltration profiling on haemodialysis-related hypotension

Yi Lun Zhou, Hui Lan Liu, Xiao Feng Duan, Ying Yao, Yi Sun and Qun Liu

Division of Nephrology, FuXing Hospital, Capital University of Medical Science, Beijing, China

Abstract

Background. Symptomatic hypotension is the most frequent complication in patients receiving haemodialysis (HD). Previous studies have reported that the use of modulating dialysate sodium concentration or ultrafiltration (UF) rates, or the combination use of sodium profile and UF profile may better preserve blood volume and reduce the incidence of hypotensive episodes. The aim of this study was to evaluate the effects of sodium balance-neutral sodium profile and UF profile and their combination on preservation of blood volume, cardiac function and occurrence of hypotensive episodes.

Methods. Using Fresenius MC 4008S, eight stable HD patients underwent four treatments: (1) control, constant dialysate sodium concentration of 138 mmol/l with constant UF; (2) sodium profile, a linearly decreasing dialysate sodium concentration (148–131 mmol/l) with constant UF; (3) UF profile, a linearly decreasing UF rate with dialysate sodium concentration of 138 mmol/l; (4) sodium + UF profile, combination of sodium and UF profile. Each treatment was applied in 10 dialysis sessions. Relative blood volume (RBV), mean blood pressure (MBP), heart rate (HR), interior vena cava diameter (IVCD), stroke volume (SV), cardiac output (CO), plasma sodium concentration and the frequency of symptomatic hypotension were monitored.

Results. There were no significant differences in the IVCD, MBP, SV, CO and body weight before dialysis between the three profiles and the control. The total plasma protein, haemoglobin, and intradialytic sodium mass removal showed similar results. Compared with the control, better preservation of RBV and MBP at 4 and 5 h and a higher stability in SV variation, but larger UF volume were achieved during sodium + UF profile (P < 0.05, respectively), the incidence of intradialytic hypotension was significantly reduced (P < 0.05).

Conclusions. With the similar intradialytic sodium removal, during sodium balance-neutral linearly decreasing sodium profile combined with linearly decreasing UF profile, greater intradialytic stability of the blood volume, blood pressure and cardiac function could be obtained, and hypotensive episodes were significantly reduced.

Keywords: blood volume monitoring; haemodialysis; hypotension; sodium balance–neutral sodium profile; ultrafiltration profile

Despite the considerable progress made in the treatment of end-stage renal failure over the last 20 years, haemodialysis (HD)-related hypotension remains a significant cause of patient morbidity. Dialysis hypotension occurring in up to 20% of dialysis sessions [1], not only causes discomfort such as muscle cramps, nausea, vomiting and lightheadedness, but also decreases the efficacy of HD [2]. Some investigators reported a correlation between blood volume changes and the occurrence of hypotension [3,4]. It has been suggested that the use of modulating dialysate sodium concentration or ultrafiltration (UF) rates or combining sodium profile with UF profile may better preserve blood volume, and thus reduce the incidence of hypotensive episodes [5–9].

Sodium profile is mainly applied with a higher dialysate sodium concentration during the early period of the session, when the blood urea concentration and urea removal is high. This tends to lessen the inevitable decrease in plasma osmolality due to urea removal and reduce the resultant shift of fluids from the outside to the inside of the cell, and then with a lower-dialysate sodium concentration during the remainder of the dialysis session to avoid sodium accumulation [10,11]. The linear, step and exponential sodium programme had been performed in studies and considered to be effective in reducing the occurrence of dialysis-related hypotension [12–14]. However, the amount of sodium...
removal was lower and interdialytic weight gain was higher in most of these studies, which would eventually lead to chronic sodium overload and hypertension. With the new technology, sodium balance–neutral sodium profiles have been made available. This means that any relative gain in sodium during the high-sodium concentration phase would be balanced automatically by an additional diffusional loss of sodium during the low-sodium concentration phase, so the risks of sodium overload during the dialysis sessions could be avoided.

UF profile is usually designed to extract the major part of the total UF volume in the first part of the session when the patient is overhydrated, to induce elevation of plasma oncotic pressure and to provide a greater driving force for vascular refilling, and thus a better blood volume preservation. Stepwise or gradual decreasing UF profiles have been studied [15–17]. A combination of UF and sodium profile was expected to improve cardiovascular stability by increasing the dialysate sodium concentration to enhance plasma refilling during periods of high UF rate and by decreasing dialysate sodium concentration when refilling appears less critical during periods of slow UF [17,18].

The aim of the present study was to evaluate the effects of sodium balance–neutral sodium profile and UF profile and the combination of sodium and UF profile on blood-volume preservation, cardiac function and occurrence of hypotensive episodes.

Materials and methods

Patients

The study was conducted in the Dialysis Centre at Fuxing Hospital, Beijing, China, from January 2003 to June 2003. Eight HD patients, under the criteria of the occurrence of hypotension in >20% of the dialysis sessions of the previous 3 months were enrolled in this study after obtaining informed consent. Otherwise, they were stable patients who had been on thrice-weekly maintenance HD for more than 6 months. The causes of end-stage renal failure were chronic glomerulonephritis (four patients), diabetes (one patient), obstructive nephropathy (one patient), hypertension (one patient) and unknown (one patient).

Exclusion criteria were cardiac or liver failure, active bleeding, peripheral vasculopathy, deep venous thrombosis, a poorly functioning fistula, or Kt/V below 1.3. If interdialytic weight gain was <1.4% of dry weight, this dialysis session was excluded from data analysis. Five patients used antihypertensive drugs such as Ca antagonists, ACE inhibitors, b-blockers, and their blood pressure at pre-dialysis was controlled between 130–160/60–90 mmHg. To minimize confounding, antihypertensive medication was withheld on the day of dialysis. During the study period, the dosage of erythropoietin was maintained unchanged.

Dialysis methods

All treatments were performed using FMC 4008S (Fresenius Medical Care AG, Bad Homberg, Germany) and polysulfone hollow-fibre dialyser F6 (Fresenius Medical Care AG), bicarbonate buffered dialysate (sodium 138 mmol/l, potassium 2.5 mmol/l, calcium 1.75 mmol/l, magnesium 0.5 mmol/l, bicarbonate 34 mmol/l). Blood flow rate was individualized from 200 to 300 ml/min. Dialysate flow rate was 500 ml/min. Dialysate temperature was 37°C. FMC 4008S made it possible to apply automatically controlled UF and sodium concentration profiles. For all studies, the prescribed dialysate sodium concentration was set at 138 mmol/l. The following four different treatments were applied to the patients: (i) control, constant sodium concentration of 138 mmol/l with constant UF; (ii) sodium profile, a linearly decreasing sodium concentration, the initial sodium concentration was always set at 148 mmol/l which resulted in the sodium concentration falling to 131 mmol/l at the end of dialysis, with constant UF; (iii) UF profile, a linearly decreasing UF rate which started at 1.33 times the rate that would be needed at constant UF with constant sodium concentration of 138 mmol/l; (iv) sodium + UF profile, combining sodium profile with UF profile. Each treatment was applied in 10 dialysis sessions. The patients were randomly allocated to one of two sequences: sequence 1, the other four patients underwent sequence 2. There is no wash-out period between the four types of treatments.

Monitoring relative blood volume

Relative blood volume (RBV) was measured with a commercially available blood volume monitor (Fresenius Medical Care), integrated in the dialysis machine. This monitor measures the transient time of short ultrasonic pulses that are sent through the blood column in the arterial line. On the basis of these measurements, the sound of velocity in the blood is calculated. The monitor further calculates the mass fraction of blood water content from the velocity and temperature. The change in the blood water content over time in turn is used for calculation of the RBV. The changes in RBV during dialysis treatment are assessed every 10 s, starting from 100% at the beginning. The values of RBV were recorded at 1 h intervals.

Patients monitoring

Blood pressure and heart rate (HR) were measured 5 min before the session (T0), 1 h (T1), 2 h (T2), 3 h (T3), 4 h (T4) during the session, at the end of the session just before extracorporeal volume infusion (T5) and on occurrence of symptoms of hypotension by Fresenius BPM. At the same time points, mean blood pressure (MBP) was calculated as (systolic pressure + 2 × diastolic pressure)/3. Patients experiencing a symptomatic decrease in supine systolic blood pressure of >30 mmHg or an absolute systolic blood pressure of <90 mmHg during dialysis, accompanied by hypotensive symptoms such as dizziness, frequent yawning or perspiration, or an event that required immediate intervention, were defined as the occurrence of symptomatic
hypotension. The instant RBV was recorded, blood volume monitoring was suspended. The treatments of the complication consisted in a reduction of UF rate or saline infusion, and, if necessary, discontinuation of the session.

Stroke volume (SV) and cardiac output (CO) were measured at T0, T1, T2, T3, T4 and T5 at the tenth session of each treatment using ultrasonography (SONOS-2500; Hewlett Packard, Palo Alto, CA). To estimate hydration status, interior vena cava diameter (IVCD) measurements were performed 5 min before dialysis at the tenth session of each treatment by the same machine. The longitudinal axis of the ICV was measured, its diameter at inspiration and at end-expiration, exactly 2 cm below the diaphragm; the IVCD was defined as a mean of IVCD at inspiration and IVCD at expiration.

Blood samples for the measurement of haemoglobin, total protein, sodium at pre-dialysis, then for the measurement of sodium at 1 h intervals during dialysis and total protein, sodium at T5 were obtained at the tenth session of each treatment. Plasma-sodium concentrations were measured by ionometry (BECKMAN LX20). Plasma–water sodium concentration (Napw) was calculated from plasma-sodium concentration (Napl) according to the following formula:

$$\text{Napw} = \text{Napl} \times \left[ \frac{100}{99.1 - 0.73 \times \text{total protein}} \right]$$

and sodium removal was calculated according to the following formula:

$$\left[ \frac{\text{final body weight} \times 0.58 + \text{total UF}}{\text{initial (Napw)}} \right] - \left[ \frac{\text{final body weight} \times 0.58}{\text{final Napw}} \right]$$

Dry body weight was determined individually by the attending physician on clinical grounds such as blood pressure, absence of peripheral and/or pulmonary oedema; IVCD 2 h after dialysis was <11.5 mm/m². Adjustments of target weight, dialysis adequacy and antihypertensive therapy were made by the unit’s attending nephrologists who were not involved in experimental design or analysis.

**Statistical analysis**

All the data were expressed as mean±SD. Analysis of variance for repeated measures was used to compare the results at each time point during the dialysis procedure with pre-dialysis values per dialysis mode. The Newman–Keuls test was applied post hoc whenever the analysis of variance indicated the presence of a statistical significance. Paired t-test was used to test for differences in the three profiled dialysis patients that were compared with the control. The incidence of hypotension in each profile was compared with the control using χ² test. Significant differences were defined as P < 0.05. All statistical analyses were performed using SPSS for Windows release 11.5 (SPSS Inc, Chicago, IL, USA).

**Results**

All eight patients completed the study. The mean age of the patients was 52±9 years, and mean duration of dialysis was 41±36 months (Table 1). A total of 331 dialysis sessions were conducted in this study. Eleven sessions were excluded from analysis data, because the patients did not meet the criterion of interdialytic weight; gain >1.4% of dry body weight; the remaining 320 sessions were analysed.
There were no significant differences in the IVCD, MBP, SV, CO and body weight before dialysis between the three profiles and the control. The total plasma protein, haemoglobin and intradialytic-sodium mass removal showed similar results. Post-dialysis body weight was reduced significantly during sodium + UF profile in comparison with the control ($P < 0.05$), along with higher UF volume ($P < 0.05$). The pre-dialysis plasma sodium concentration did not differ between the three profiles and the control, neither did the post-dialysis sodium concentration.

The pre-dialysis plasma sodium concentration did not differ between the sodium profile and the control, but was significantly lower than the control ($P < 0.05$). The variation in SV during the sodium profile was similar to the control, the significant decrease was from point T3 onwards. The significant decreases during the control and the sodium profile were from point T4 onwards compared with the beginning. The sodium + UF profile was associated with greater stability of the MBP, the significant lower value in comparison with the beginning was observed at point T5 only, the differences between the sodium + UF profile and the control were most pronounced at points T4 and T5 ($P < 0.05$, for each), noticeably the moment when most hypotensions occur (Figure 3).

HR showed a stable trend during the sodium + UF profile, but was significantly lower than the control only at point T5. HR increased similarly during the four treatments and the significant increases compared with pre-dialysis values, were all from point T3 onwards (Figure 4).
Intradialytic hypotension was significantly reduced during the sodium + UF profile as compared with the control ($P < 0.05$), the incidence of hypotension during the sodium profile or during the UF profile was similar to the control (Figure 5).

**Discussion**

The incidence of intradialytic hypotension is still very high despite continuous improvements in dialytic technologies. Dialysis-induced hypovolaemia is considered the major causal factor. Change in effective blood volume depends on the equilibrium between fluid moving outside the body by UF and vascular refilling from the interstitial space. Plasma refilling rate varies directly with tissue hydration, cardiovascular status, plasma total protein and haemoglobin, sodium concentration of the dialysate, etc. Sodium profile, UF profile and the combination of sodium and UF profile were designed to improve vascular refilling and thereby dialysis tolerance. In this study, every patient was his or her own control, and they did not differ significantly in the IVCD, MBP, HR, SV and CO before dialysis between the three profiles and the control, so comparability was achieved in the hydration and cardiac status pre-dialysis. The intradialytic-sodium mass removal during the three profiles was similar to the control, so any results of this study were not achieved at the expense of intradialytic-sodium overload.

During the sodium profile, a linearly decreasing dialysate sodium concentration from 148 to 131 mmol/l resulted in a higher plasma sodium concentration at the first hour ($P < 0.05$), and better preservation of RBV was expected in the first half of the session with relative higher sodium concentration, but in this study, the RBV decrease did not improve during the sodium profile compared with the control. No benefits could be found in the variation of SV and MBP. At the end of the session, the RBV did not differ between the two treatments, neither did the incidence of hypotension. At an equal intradialytic sodium removal, the effects of sodium profiles on RBV and blood pressure were controversial. B. Straver et al. [16] reported that eight patients used sodium-balanced decreasing sodium-profile, containing a dialysate conductivity of 15.2 mS/cm in the first hour, followed by 13.7, 14.5, 14 mS/cm in the remaining 3 h, respectively. Blood pressure preservation was improved, due to a better SV preservation early in dialysis, but without a significant reduction in blood volume decrease. However, no effect on blood pressure but better preservation of blood volume with a decreasing sodium concentration profiling vs constant dialysate sodium was found in 10 patients with an equal negative sodium balance in another study [5]. One recent study using Fresenius MC 4008H step-down sodium profile (the starting sodium concentration was set at 145 mmol/l) in 11 patients failed to improve dialysis tolerance [17]. The different results may be owing to the difference in modelling and the study period. In the first two studies as indicated above, sodium profile and standard HD were only applied once in each patient. Whereas the RBV changes during HD had a considerable intra- and inter-individual variability that could not be explained by differences in UF volume [18], long-term studies with large samples are needed to demonstrate the effect of different sodium profiles on RBV and hypotension.

Using a linearly decreasing UF rate started at 1.33 times the rate for constant UF in this study, the decrease of RBV was significantly steeper due to the vigorous UF rate in the first half of the session. There was a significant reduction of SV compared with pre-dialysis levels from the second hour to the end, which might be a result of decreased cardiac perfusion related to hypovolaemia. Though at the end of the session RBV, SV and CO of UF profile and the control were not significantly different, more insignificant events of hypotension were found during the UF profile. The high occurrence of hypotension might be due to the rapid reduction in blood volume in the early phase which may result in higher tissue ischaemia and a higher sympathetic outflow [19]. The former induces
a higher connected induction of hypotension through the impairment of peripheral vascular resistance; the latter induces a lack of sympathetic outflow which may decrease the peripheral vascular resistances. Johannes Donauer et al. [15] reported that, compared with standard HD, better haemodynamic stability and a reduction in the frequency of hypotension (5.7% vs 13.3% $P > 0.05$) were found with the linearly decreasing UF rate (Fresenius 4008S) in 53 patients. In contrast, the use of UF profiling with intermittent UF rate more than 1.5 times average UF increased the incidence of hypotension significantly. The tendency of a decrease in RBV during phases with high UF rates was considered to be related to the high incidence of hypotension. The tolerance of high UF rate varied individually and may be responsible for the different results, but Donauer’s opinion that rapid lowering of RBV from the initial stage may be correlated with the increase of hypotensive episodes was in accordance with ours. Joon Ho Song et al. [17] also observed no improvement in intradialytic discomfort when 11 patients used Fresenius MC 4008H stepwise decreasing UF profile (UF rate began with $1.5 \times$ UF rate). In another study with decreasing UF profile, whereby 40% of the total UF volume was removed in the first hour, no beneficial effect on intradialytic haemodynamics was found [16]. A volume-controlled biofeedback system, adjusting the UF rate to avoid the rapid decrease of blood volume may be useful in reducing the occurrence of hypotension [20].

During the sodium + UF profile, a more stable variation of RBV and cardiac function (in terms of SV and CO maintenance), was associated with greater stability of the MBP and HR. The occurrence of intradialysis hypotension was significantly decreased ($P < 0.05$). It is worth mentioning that these results were obtained under the same sodium mass removal, but relatively higher UF volume ($P < 0.05$) which may result from the improved dialysis tolerance, lowering the frequency of reducing UF volume or early discontinuation of the session. Venous compliance is usually reduced in HD patients, especially when they have hypertension [21], so even a small improvement in blood-volume preservation might lead to enhanced SV, due to the delicate relation between filling of the heart and CO, along with improvement of blood pressure. The stability of the heart rate during the sodium + UF profile confirms the lower sympathetic outflow induced by this technique, thanks to the stabilizing effect on blood volume. Few studies combining sodium and UF profiles that kept total amounts of sodium removal identical to that of standard dialysis treatment have been performed, and the results are still debated. Iselin et al. [22] reported no benefits on the occurrence of hypotension or on the preservation of blood volume in seven patients using Fresenius MC 4008S with a linearly decreasing sodium profile (sodium concentration from 145 to 133 mmol/l) adapted to a linearly decreasing UF profile. Splendiani et al. [9] observed eight patients with a progressive decrease of UF together with a variable conductivity of $-0.2, +0.2, +0.6, +0.6, 0, -0.4, -0.4$ and $-0.4$ mS/s, and found a lower incidence of hypotension with better cardiovascular stability, but no effect on blood volume at the end of dialysis. Joon Ho Song et al. [17] reported 11 patients using Fresenius MC 4008H step-down sodium profile (the starting sodium concentration was set at 145 mmol/l) combined with the stepwise decreasing UF profile (UF rate began with $1.5 \times$ UF rate) obtained reduction of intradialytic discomforts. At present, these studies are still small samples, if the difference in tissue hydration and cardiovascular status is taken into consideration; more studies of different models should be performed. In the future, the combined use of blood volume and sodium kinetic monitoring within a closed-loop biofeedback system may enable the clinician to adjust both the UF rate and the dialysate sodium concentration in order to reach the target UF volume within predetermined safe blood volume margins with identical sodium removal.
Sodium, ultrafiltration profiling and haemodialysis-related hypotension

Such an approach may be of great importance in reducing intradialytic hypotensive episodes [23,24].

In conclusion, with the similar intradialytic sodium balance, greater intradialytic stability of the blood-volume and cardiac function could be found during sodium balance–neutral linearly decreasing sodium profile combined with linearly decreasing UF profile, hypotensive episodes were significantly reduced. Sodium profile or UF profile as mono-therapy has no beneficial effect on intradialytic haemodynamics. Our results indicate that the combination of the above profiles may represent an efficient approach to decrease dialysis-related hypotension, but long-term studies with large samples from clinical practice should be done to confirm the efficacy before it becomes a routine procedure.

Conflict of interest statement. None declared.

References


Received for publication: 29.3.06
Accepted in revised form: 30.5.06