Do Changes in Relative Blood Volume Monitoring Correlate to Hemodialysis-Associated Hypotension?

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Key Words

Relative blood volume monitoring • Hematocrit • Bioimpedance • Extracellular fluid • Hemodialysis

Abstract

Introduction: Intradialytic hypotension remains the most common complication for outpatient hemodialysis, and relative blood volume monitoring was designed to reduce hypotension. Reports of the usefulness of this technology, however, have been variable. **Methods:** We audited the usefulness of relative blood volume monitoring recorded throughout the mid-week dialysis in 72 stable adult outpatients who had multifrequency bioimpedance measurements. **Results:** The blood volume measurement (BVM) at the end of the session was $91.6 \pm 0.6\%$ and was not different from the nadir BVM recorded (90.7 ± 0.5). The BVM was strongly correlated with change in hematocrit ($r = -0.56$, $p < 0.001$) and albumin ($r = -0.69$, $p < 0.001$), but had no relationship with pre-, intra- or postdialysis blood pressure recordings. The BVM was not associated with ultrafiltration volume, but did correlate with a postdialysis change in extracellular fluid volume ($r = -0.39$, $p = 0.006$). **Conclusion:** In this audit, although the BVM at the end of the dialysis session was correlated with changes in hematocrit, serum albumin and extracellular fluid volume, the change in the relative BVM did not mirror changes in intradialytic blood pressure.

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Introduction

Over the past four decades, hemodialysis has become an outpatient-based chronic treatment for patients with chronic kidney disease, with the majority of patients now dialyzing without direct medical supervision [1]. Intradialytic hypotension is the most commonly reported adverse effect of outpatient hemodialysis [1, 2]. To try and prevent intradialytic hypotension, advances in dialysis machine technology introduced relative blood volume measurement (BVM), based on the passage of light or sound waves through a column of blood. During hemodialysis, ultrafiltration reduces plasma water increasing hematocrit, which is then detected by the BVM module and reported as a fall in relative blood volume.

It was hoped that this technology would reduce the incidence of intradialytic hypotension by detecting falls in relative plasma volume that preceded hypotension, thus allowing preventative interventions. Initial studies reported a reduction in intradialytic hypotension [3, 4]. However, these encouraging results were not uniformly reproduced in larger multicenter clinical trials [5, 6]. Refinements in technology led to the development of automated ‘fuzzy logic’ systems with the capability to continuously monitor relative blood volume during dialysis and individualize ultrafiltration rates accordingly. Again, initial studies using this ‘fuzzy logic’ technology approach observed a reduction in the frequency of serious

intradialytic hypotensive episodes in patients prone to intradialytic hypotension [7, 8]. However, other trials have suggested that changes in relative blood volume markedly underestimate the changes in total blood volume which occur during dialysis sessions [9].

To assess the usefulness of relative blood volume monitoring, we prospectively audited changes in relative blood volume in a cohort of healthy chronic hemodialysis outpatients to determine whether there was any correlation with intradialytic hypotension.

Methods and Patients

72 adult patients, 50% male, mean age 55 ± 2.0 years, 36.1% diabetic with 20.8% prescribed insulin, attending for routine outpatient dialysis in a university dialysis center were studied during a routine mid-week outpatient hemodialysis session. Patients with implantable defibrillators and resynchronization pacemakers were excluded, as were patients unable to stand on the bioimpedance machine. Median dialysis vintage was 23 months (8.5–48 months). All patients dialyzed with high-flux polysulphone dialyzers (Fresenius, Bad Homburg, Germany) [10] using bicarbonate dialysate (35 mEq/l) containing 1 g/l glucose, with a median dialysate sodium of 136 mEq/l (interquartile range: 136–138 mEq/l), calcium 2.65 mEq/l (2.0–2.7) and a dialysate temperature of 35–36°C. The mean dialysis session time was 3.78 ± 0.85 h, with an on-line Kt/V of 1.61 ± 0.26 , and both relative blood volume monitoring and integrated blood pressure were recorded (Fresenius 4008, Fresenius, Bad Homburg, Germany). Constant ultrafiltration rate profiles were used in all cases, with a mean rate of 7.2 ± 0.4 ml/kg/h; no patient received ultrafiltration profiling or had ultrafiltration stopped. Patients refrained from eating during the dialysis session, but were allowed to drink up to 180 ml of fluid. Multifrequency bioimpedance was performed prior to and 20–30 min after dialysis using an eight-contact electrode system (Biospace in Body 720, Seoul, South Korea) [11]. This equipment has been validated [12] and has a coefficient of variation for the ratio of fluid volumes within the right and left arms of hemodialysis patients of 1.59 and 1.7%, respectively [13]. Serum biochemistry samples were analyzed with a standard multichannel biochemical analyzer (Roche Integra, Roche Diagnostics, Lewes, UK), using the bromocresol green method for albumin determination and hemoglobin (XE-2100 Sysmex Corp., Kobe, Japan). 24-hour urine collections were analyzed to determine urine volume and sodium content. Plasma osmolality was calculated in SI units using $1.8 \times$ (sodium and potassium mmol/l) plus glucose and urea (mmol/l). All patients had received standard dietary advice by a qualified renal trained dietician.

Ethical approval was granted by the local ethical committee as audit and clinical service development, as multifrequency bioimpedance had been introduced into routine clinical practice in 2008.

Statistical Analysis

Results are expressed as means $\pm$ SD, medians and interquartile ranges, or percentages. Statistical analysis was done by a Stu-

Table 1. Change in weight, blood pressure, intracellular and extracellular fluid volumes following hemodialysis

	Predialysis	Postdialysis
Weight, kg	68.3 ± 1.8	66.9 ± 1.7
Systolic blood pressure, mm Hg	147.2 ± 3.3	138.0 ± 3.0
Diastolic blood pressure, mm Hg	79.4 ± 2.2	75.6 ± 1.9
Hematocrit, %	35.7 ± 0.006	37.9 ± 0.006
Serum albumin, g/l	40.5 ± 0.5	43.6 ± 0.7
Serum sodium, mmol/l	139.8 ± 0.3	140.7 ± 0.2
Serum glucose, mmol/l	7.6 ± 1.0	6.8 ± 0.2
Sodium gradient, mmol/l	3 (1–6)	4 (2–5)
Intracellular water, liter	21.9 ± 0.6	21.2 ± 0.6
Extracellular water, liter	14.2 ± 0.4	13.2 ± 0.3

Mean $\pm$ SEM, or median (interquartile range). Sodium gradient is the difference between serum sodium and dialysate sodium.

dent's paired t test for parametric and the Wilcoxon rank-sum pair test for nonparametric data, with the Bonferroni correction for multiple analyses where appropriate (Graph Pad Prism version 3.0; Graph Pad, San Diego, Calif., USA). Simple regression analysis was performed with Pearson's rank correlation and logistical linear regression analysis was undertaken with SPSS version 15.0 (SPSS, Chicago, Ill., USA). Statistical significance was taken at or below the 5% level.

Results

The mean relative BVM at the end of the dialysis session was $91.6 \pm 0.6\%$, and the nadir recorded $90.7 \pm 0.5\%$. The mean change in weight following dialysis was 1.83 ± 0.09 kg, or $3.06 \pm 0.16\%$ weight loss, with a mean percentage change in total extracellular water of 1.0 ± 0.09 l, or $6.93 \pm 0.5\%$ (table 1). The mean difference between predialysis serum sodium and dialysate sodium was 2.9 ± 0.5 mEq/l. The median CRP for the cohort was 5 mg/l (2–13.5). 50% of patients were prescribed blood pressure medications, with the median number of medications being 1 (1–2); 35.3% β -blockers; 23.6% angiotensin receptor blockers; and 25% angiotensin-converting enzyme inhibitors. The median 24-hour urine output for the cohort was 0 ml/day (0–940) with a median urinary sodium excretion of zero (0–65 mEq/day).

Seventeen patients had a fall in systolic blood pressure of ≥ 20 mm Hg, but no patient was symptomatically hypotensive or received parenteral fluids. Prior to dialysis this group had a higher systolic blood pressure (table 2), but there were no differences in ultrafiltration rate or

Fig. 1. Correlation between change in hematocrit and BVM recorded at the end of the dialysis session.

Fig. 2. Correlation between percentage change in extracellular water volumes and BVM recorded at the end of the dialysis session.

Table 2. Predialysis values or changes during the dialysis session in the hypotensive and nonhypotensive groups

	Hypo- tensive	Nonhypotensive
Predialysis SBP, mm Hg	159.8 ± 6.4	145.4 ± 4.7
Change in SBP, mm Hg	-32.8 ± 2.6	2.4 ± 2.6***
UF rate, ml/kg/h	7.8 ± 0.8	6.9 ± 0.5
Predialysis serum sodium, mmol/l	139.8 ± 0.9	140.1 ± 0.4
Dialysate sodium, mmol/l	136.6 ± 0.3	137.3 ± 0.3
Sodium gradient, mmol/l	3.18 ± 0.9	2.77 ± 0.6
% change in BVM	-6.8 ± 1.1	-7.5 ± 0.7
% change in ECW	-6.73 ± 0.87	-7.03 ± 0.6
% change in ICW	-3.24 ± 0.9	-4.44 ± 1.2

Mean ± SEM. Sodium gradient = serum sodium – dialysate sodium. SBP = Systolic blood pressure; UFR = ultrafiltration rate; ICW = intracellular water volume; ECW = extracellular water volume. *** $p < 0.001$.

change in relative blood or change in extracellular fluid volume (table 2).

There was a close correlation between the BVM at the end of dialysis and the lowest recorded during dialysis (nadir; $r = 0.84$, $p < 0.0001$). As for 27 patients (38%), the nadir BVM was that recorded at the end of dialysis session. The median difference between the nadir and end-of-dialysis BVM was 0.55% (0–1.75) with an absolute range of 0–18.1%. As expected, there was a negative correlation with the change in hematocrit (fig. 1) and serum

Table 3. Simple correlation analysis for the relative BVM recorded at the end of dialysis, or the lowest recorded during the hemodialysis session (nadir)

	BVM end		BVM nadir	
	r	p	r	p
Δ serum albumin	-0.536	0.000	-0.646	0.000
On-line Kt/V	-0.399	0.001	-0.393	0.002
24-hour urine volume	0.36	0.002	0.35	0.0026
Δ ECFht ¹	-0.348	0.003	-0.411	0.000
% Δ ECF R arm	-0.282	0.017	-0.30	0.011
% Δ ECF L arm	-0.279	0.017	-0.279	0.018

¹ Change in extracellular fluid corrected for height (Δ ECFht), and relative change in body compartments in the right and left arms.

albumin ($r = -0.69$, $p < 0.001$), but not the change in serum osmolality. However, there was no relationship between either the nadir BVM or BVM recorded at the end of the dialysis session and blood pressure, whether it was predialysis, postdialysis or intradialytic nadir, systolic, diastolic or mean arterial pressure, nor was there a correlation with the ultrafiltration rate or serum sodium to dialysate sodium gradient. There was a correlation between the percentage change in extracellular water measured by multifrequency bioimpedance and both the nadir and end-of-session BVM (table 3; fig. 2). There was a correlation between increasing Kt/V and a lower BVM,

and residual renal function with a higher BVM. Assessment of body compartments showed a correlation between the change in extracellular fluid volumes in the arms and BVM (table 3), but not for the legs or trunk. There was no statistical relationship between changes in extracellular fluid volumes (including when corrected for height or body surface area) or changes in body compartment fluid volumes and pre-, intra- or postdialysis blood pressure.

Logistical regression was performed using those variables which were significantly correlated with the nadir and post-session BVM on univariate analysis, to which age, sex, dialysis vintage and diabetes were added, and then analyzed in a backwards step fashion. Only the change in serum albumin had a consistent relationship with both the end-of-session BVM and nadir BVM (model r^2 0.48, β -0.359, standard error 0.075, 95% CI -0.509 to -0.21, F 13.3, p = 0.001).

Discussion

There are many causes of intradialytic hypotension [1], although reduced effective plasma volume due to a relative difference in ultrafiltration and plasma refilling rates is probably the most common [2], particularly towards the end of the dialysis session. Relative blood volume monitoring was introduced with the hope of predicting and preventing this common complication of hemodialysis treatment. Early devices detected changes in blood volume mainly through indirect measurement of hematocrit; therefore, the close correlations observed between blood volume monitoring and the changes in hematocrit and serum albumin were to be expected. There are some technical differences between the different systems currently in practice [14]. In particular, the Fresenius system used in our study monitors blood volume by detecting changes in blood density, and this probably accounts for the stronger correlation observed between blood volume monitoring and percent change in albumin than that with percent change in hematocrit.

In our audit the nadir-relative BVM was the same as the BVM recorded at the end of the dialysis session in some 38% of patients, with little difference between the end-of-session and nadir BVM. There was a simple correlation between the fall in extracellular fluid volume, as measured by multifrequency bioimpedance, and the decrease in the BVM during the dialysis session, in keeping with earlier studies using single frequency bioimpedance measurements [15], although this relationship was not as

strong as for the increase in hematocrit and serum albumin.

It has been suggested that patients more prone to intradialytic hypotension have a relatively increased amount of extracellular fluid in the arms, relative to the trunk, compared to that in the legs [16]. In our study, segmental analysis showed a weak correlation between the changes in the BVM and extracellular water in the arms, but not with larger compartments, such as the trunk and legs. This may be due to a size effect, as the amount of extracellular water retained between dialysis sessions is less in the arms than in the legs and trunk [16, 17]. In addition, this is in keeping with the previous results from Dasselaar et al. [9] who reported that the change in total blood volume during a hemodialysis session was twice that detected by relative blood volume monitoring.

Patients who still retained some degree of renal function were more likely to have a higher relative BVM at the end of dialysis, suggesting that less volume had been removed during dialysis. There was an apparent relationship between on-line Kt/V and the BVM, which may have been due to an increased ultrafiltration component leading to a lower BVM, as there was no association with session time.

As with several other studies, we were unable to demonstrate any relationship between changes in the relative BVM and intradialytic blood pressure [6]. In particular, the group of patients with a fall in systolic blood pressure of 20 mm Hg or more did not differ in terms of fluid removed or change in the BVM. However, we were auditing our outpatient patient population and not specifically targeting a group of hypotensive prone patients. Compared to some other reports, ultrafiltration volumes were modest [18] and patients dialyzed using cooled dialysate, and the effect of cooled dialysate may have reduced any effect of a serum-to-dialysate sodium gradient [19, 20]. It therefore remains to be determined whether our results are equally applicable to patients with recurrent intradialytic hypotension.

Changes in blood pressure occurring during dialysis may be multifactorial, including changes secondary to a reduction in vascular tone [21], potentially exacerbated by autonomic dysfunction, particularly in diabetic subjects [22], rather than simply due to ultrafiltration alone. The unexpected lack of correlation between the BVM and ultrafiltration volume could potentially be explained by redistribution of extracellular fluid between compartments during hemodialysis. Therefore, although the total extracellular fluid volume decreases, hypotension may be

avoided provided that the intravascular compartment volume is maintained.

This is supported by recent studies which have shown that ultrafiltration during dialysis leads to a reduction in plasma volume with compensatory refilling that is initially due to vasoconstriction of the small capillaries and subsequently arterioles [23]. As the hematocrit in capillaries is lower than that in the inferior vena cava, the plas-

ma compartment is initially refilled with relatively more plasma water, which will reduce the apparent rise in hematocrit during dialysis [9]. Thus, sensing systems based solely on change in hematocrit could therefore potentially underestimate the effect of ultrafiltration on effective plasma volume, and this may partly explain the lack of any relationship observed with peridialysis blood pressure [24].

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