Predicting episodes of hypotension by continuous blood volume monitoring among critically ill patients in acute renal failure on intermittent hemodialysis

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Research support: Gambro Canada, Canadian Association of Critical Care Nurses

Key words: acute renal failure, intermittent hemodialysis, blood volume monitoring, critically ill

Abstract

Background: *Acute renal failure (ARF) develops in 23% of all critically ill patients. Hypotension occurs in 25% to 50% of patients during intermittent hemodialysis (IHD) for ARF. Blood volume (BV) monitoring has been used in chronic renal failure, with limited use in ARF during IHD. Continuous BV monitoring in the stable critically ill patient with ARF could predict, and possibly prevent, development of hypotensive episodes.*

Methods: *This prospective observational study examined the relationship of BV and BV slopes to hypotension in 11 critically ill adults with ARF over three consecutive IHD Runs. The hypothesis was that there is a patient-specific critical BV and/or a specific BV slope that indicates forthcoming hypotension.*

Results: *The incidence of hypotension, according to mean arterial pressure < 70 mmHg, was 70%. No relationship was found between BV and blood pressure, and occurrence of hypotension in critically ill patients with ARF on IHD.*

Conclusion: *Monitoring BV was not shown to predict hypotension in this cohort dialyzed via central venous catheters.*

Critically ill patients are at high risk (23%) of developing acute renal failure (ARF) secondary to their presenting problem of shock, trauma or vascular disease (Lameire & Vanholder, 2000; Mehta, 1994). Critically ill patients who develop ARF have a 35% to 50% increase in mortality (Lameire, Van Biesen, Vanholder, & Colardijn, 1998). One treatment modality for ARF in the critically ill patient has been intermittent hemodialysis (IHD); however, a major complication of IHD is hypotension (Conger, 1998). Hypotension occurs in approximately 50% of critically ill patients with ARF on IHD (Mehta, 1994). The occurrence of dialysis-induced hypotension may be multifactorial. Changes in plasma osmolality, autonomic neuropathy, and loss of vasoactive substances such as catecholamines are associated with dialysis-induced hypotension. The ultrafiltration rate (UFR) is a major factor in dialysis-induced hypotension. The inability of the body to equal the UFR with fluid obtained by plasma refill leads to decreased intravascular volume causing hypotension (Sturniolo, Costanzi, Ruffini, Passalaqua, Fulignati, & Splendiani, 1990). Thus, Lopot, Kotyk, Blaha, and Forejt (1996) described a continuous blood volume (BV) monitoring technique that could be used to detect the risk of hypotension. Theoretically, by monitoring BV, one should be able to predict episodes of hypotension.

Research to date supports the benefit of continuous BV monitoring in the chronic renal failure (CRF) patient (deVries et al., 1993; deVries, Donker, & deVries, 1994; Steuer, Harris, & Conis, 1993), especially in the hypotensive prone patient (Donauer, Kolbin, Bek, Krause, & Bohler, 2000; Steuer, Leypoldt, Cheung, Harris, & Conis, 1994). Donauer et al. (2000) also indicated that BV monitoring was only effective in predicting hypotension in patients with hypovolemic hypotension (Type 1) and not with patients with hypotension caused by cardiovascular dysfunction (Type 2). Recent research indicates that the patient's critical BV threshold, the specific value whereby hypotension occurs, must be determined for the patient to benefit from BV monitoring in the prevention of dialysis-induced hypotension (Howard, Palmer, Howard, Goldberger, & Shabshab, 1998; Steuer, Leypoldt, Cheung, Harris, & Conis, 1994; Steuer, Leypoldt, Cheung, Senekjian, & Conis, 1996). However, the use of BV monitoring has not been studied as intensely in the critically ill patient with ARF requiring IHD. Critically ill patients with ARF are frequently catabolic, hemodynamically unstable, and often have substantial fluid volume excess (Paganini, Sandy, Moreno, Kozlowski, & Sakai, 1996). In addition to their underlying disease, they frequently have compromised cardiovascular compensatory mechanisms (Paganini et al., 1996). They require efficient

and carefully planned hemodialysis to provide optimal renal support (Conger, 1998). The need for stable dialysis in the critically ill patient with ARF has been emphasized, as dialysis-induced hypotension may be responsible for prolongation of ARF by potentially re-insulting the kidneys (Conger, 1998). However, Tonelli, Astephen, Andreou, Beed, Lundrigan, and Jindal (2002) were unable to predict hypotensive episodes in the critically ill patient in ARF on IHD. So, the question remains as to whether continuous BV monitoring in the stable critically ill patient with ARF can predict hypotensive episodes. If this relationship exists, monitoring BV and BV slopes could possibly prevent development of hypotensive episodes in the critically ill ARF patient.

Purpose

The purpose of this study was to examine the relationship of BV and BV slopes to hypotension in the critically ill ARF adult patient on IHD admitted to a general systems intensive care unit (GSICU). The hypothesis was that there is a patient-specific critical BV and/or a specific BV slope that indicates forthcoming hypotension.

Methods

Design. A prospective observational design (within subject repeated measures) of 11 patients for a total of 33 IHD runs was used to examine the relationship of BV and BV slopes to the development of hypotension in the critically ill ARF patient on IHD. BV, heart rate (HR), systolic blood pressure (SBP), and mean arterial pressure (MAP) were obtained every 15 minutes for three consecutive dialysis sessions occurring either daily or every second day. The length of the dialysis was determined by the intensivist based on an estimation of the amount of time required for adequate clearance of uremic toxins and safe removal of fluid in order to avoid hypotension. The length of IHD Run ranged from four to seven hours and varied between the IHD runs, with six hours being the most common. The UFR and dialysate osmolality (sodium concentration of dialysate bath was set at 140) were constant throughout the IHD run. The dialysate flow rate was 500 mls for all patients. The dialysate temperature was maintained at the current standard of 37 degrees Celsius or one degree cooler than the patient's body temperature. All IHD runs were done through a dual lumen central venous catheter. Ethical approval was obtained for conduct of the study.

Sample. The sample consisted of hemodynamically stable critically ill patients > 18 years of age with ARF. Patients were excluded if they were on IHD for isolated hyperkalemia not caused by ARF, on IHD for drug overdose, on IHD with a diagnosis of chronic renal failure, or receiving blood transfusions during IHD. There were 59 patients admitted to GSICU during the 10-month data collection period who required IHD. Of these 59 patients, 44 patients did not meet the inclusion criteria, and 15 patients provided informed consent and were enrolled in the study. Analysis was completed on 11 patients, as one patient withdrew consent and three patients had ARF resolve prior to completion of data collection.

Definition of variables. Hypotension, BV slope, and critical BV were defined as follows:

Hypotensive episode was a SBP < 90 mmHg or a decrease of ≥ 30 mmHg and/or a MAP < 70 mmHg (Sturniolo et al., 1990; Tonelli et al., 2002). Hemodynamically unstable

Table One: Patient characteristics (n=11)

Characteristic	Frequency	(%)
Age		
18-30	2	(18.2)
31-50	2	(18.2)
51-70	5	(45.5)
71-90	2	(18.2)
Gender		
Male	7	(63.6)
Female	4	(36.3)
Admission Diagnosis		
Respiratory Failure	4	(36.4)
Sepsis	2	(18.2)
Trauma	1	(9.1)
Abdominal Surgery	3	(27.3)
Cardiac Disease	1	(9.1)
Admission Apache II Scores		
1-20	4	(36.4)
21-30	5	(45.5)
>30	2	(18.2)
Comorbidities		
Diabetes Mellitus	1	(9.1)
Cancer	2	(18.2)
Cancer & HTN*	1	(9.1)
Vasculitis	2	(18.2)
Renal Insufficiency, CAD* & Diabetes Mellitus	3	(27.3)
Psychiatric	1	(9.1)
None	1	(9.1)
Etiology of Renal Failure		
Rhabdomyolysis	3	(27.3)
Acute Tubular Neurosis	5	(45.4)
Vasculitis	1	(9.1)
Acute on Chronic Renal Failure	2	(18.2)
Previous Dialysis Treatment		
IHD*	4	(36.4)
CRRT*	5	(45.5)
IHD/CRRT*	2	(18.2)
Body Mass Index		
20-30	6	(54.4)
31-40	3	(27.3)
41-50	2	(18.2)

* CAD = Coronary Artery Disease, HTN = Hypertension, IHD = Intermittent Hemodialysis, CRRT = Continuous Renal Replacement Therapy

patients who required initiation of vasopressors or titration of vasopressors to maintain a SBP ≥ 90 mmHg were identified as having a hypotensive episode. The BP had to return to normal for greater than five minutes to be considered a new hypotensive episode. BP and/or MAP was measured by arterial line or BP cuff and documented on the patient's hemodialysis log. BV was monitored continuously by an optical reflection method on the Integra dialysis machine (Hemoscanning). BV was obtained at 15-minute intervals, and prior to hypotension, for each dialysis session.

BV slope is a tracing of BV over time during the IHD run. BV slope was obtained from a graph generated by continuous BV monitoring on the Integra dialysis machine. BV slopes can be flat, linear decrease, concave upward increase, or concave downward decrease (Andrulli, Colzani, Mascia, Lucchi, Stipi, Bigi, et al., 2002). The BV slope for each IHD run was classified independently by two raters.

Critical BV is the decrease of BV below a specific value whereby hypotension occurs. To obtain the critical BV, the BV at each hypotensive episode during the three IHD runs was averaged to obtain the critical BV for that patient (Begin, Deziel, & Madore, 2002).

Data analysis. Descriptive statistics were conducted for all variables. Critical BV was calculated by averaging the BV prior to each hypotensive episode during the three IHD runs. Inter-rater reliability of BV slope classification was assessed using a Kappa statistic. Frequency of hypotensive episodes was calculated per BV slope classification. The relationship between BV and BP (MAP and SBP) was examined using linear regression analysis, and Chi-square analysis was done to examine the relationship of BV slope to frequency of hypotensive episodes.

Findings

Analysis was completed on 11 patients for a total of 33 IHD runs. The mean age of the patients was 55.73+ 20.6 years, with a range of 19 to 87 years. The most frequent admitting diagnosis was respiratory failure (36.4%), and the most frequent comorbidity was a combination of renal insufficiency, coronary artery disease, and diabetes mellitus (27.3%). The mean Apache II Score was 22.73 ± 6.69, with a range of 13 to 33. The most common etiology of ARF was acute tubular necrosis due to shock (45.5%), followed by rhabdomyolysis (27.3%). All patients received some form of hemodialysis prior to enrollment in the study, the most common being continuous renal replacement therapy (CRRT) (45.5%) (Table One).

The overall incidence of hypotension according to MAP was 70%, and according to SBP was 34%. The frequency of hypotensive episodes by MAP in both IHD run one and IHD run three was 63.6%, and 81.8% in IHD run two; by SBP was 36.4% in IHD run one, 72.7% in IHD run two, and 27.3% in IHD run three. Although the frequency of hypotension by MAP was high, no treatment occurred in 63.6% of the hypotensive episodes in IHD run one and IHD run two, and in 72.7% in IHD run three. The mean heart rate ranged from 87.91 ± 16.54 beats per minute (BPM) pre-IHD run one to 81.82 ± 13.71 BPM pre-IHD run three. The mean heart rate at completion of the IHD runs was comparable, with a mean of 90.36 ± 18.09 BPM post IHD run one to 86 ± 14.92 BPM post-IHD run three.

The BV slope for each IHD run was classified independently by two raters. Inter-rater agreement for IHD run one was k=0.554, for IHD run two was k=0.033, and for IHD run three was k=0.542. The overall percentage agreement between the raters was 51% (17 out of 33). The most frequent BV slope was linear decrease, with a rate of 63.6% in IHD run one, 45.5% in IHD run two, and 54.5% in IHD run three. The next most common BV slope was concave upwards decrease at 9.1% in IHD run one, and 27.35% in both IHD run two and IHD run three; followed by flat at 27.3% in IHD run two, and 9.15% in both IHD run one and IHD run three. Concave downwards decrease occurred only once in IHD run three. There was no significant relationship found between BV slope and hypotensive episodes per IHD run in this cohort.

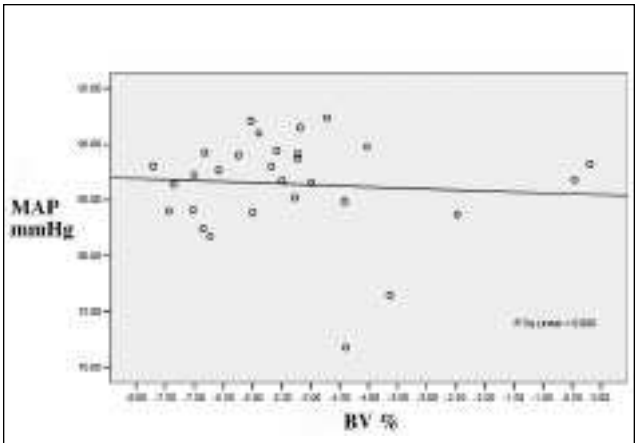

Figure One: Relationship between Mean Arterial Pressure (MAP) and Blood Volume (BV%)

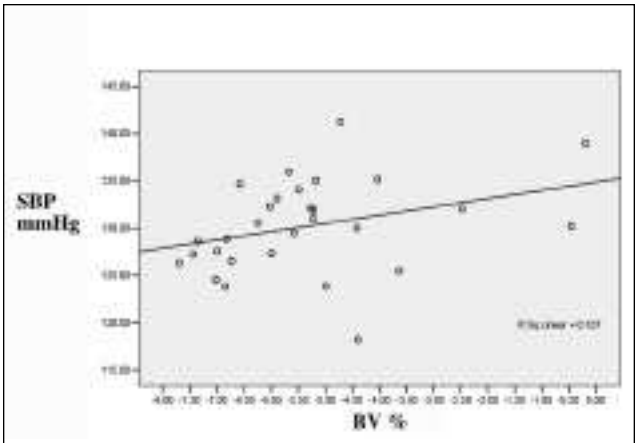

Figure Two: Relationship between Systolic Blood Pressure (SBP) and Blood Volume (BV%)

Linear regression was done to determine if there was a relationship between blood volume and blood pressure during IHD runs. With the dependent variable as MAP, and the independent variable as BV, there was a correlation of 0.075, accounting for 0.60% of the variance (p=0.70) (Figure One). With the dependent variable as SBP, and the independent variable as BV, there was a correlation of 0.327, accounting for 11% of the variance (p=0.08) (Figure Two). Thus, BV did not predict BP in this cohort.

The critical blood volume (CBV) was calculated for 10 patients who experienced hypotension. A linear regression was also done to determine the relationship of CBV and blood pressure. With the dependent variable MAP, and independent variable BV, there was a correlation of 0.144, accounting for 2.10% of the variance (p=0.083) (Figure Three). With SBP as the dependent variable and BV as the independent variable, there was a correlation of 0.151, accounting for 2.30% of the variance (p=0.068) (Figure Four). Thus, a CBV was not determined to be predictive of hypotension.

Discussion

Hypotension. Ten of the 11 patients experienced hypotension during hemodialysis. The incidence of hypotension over all three IHD runs according to MAP <70 mmHg was 70%, higher than the 30% reported by Tonelli et al. (2002). The incidence of hypotension according to SBP <90 mmHg was 45% over all three IHD runs, also higher than the 18% reported by Tonelli et al. (2002). This is an interesting finding as the average length of dialysis run in this study was longer than most. Therefore, we would have expected the frequency of hypotensive episodes to be lower. Studies with IHD runs >4 hours have shown a decreased frequency of hypotension in ARF patients on dialysis in GSICU (Kumar, Craig, Depner, & Yeun, 2000). It is possible that the small sample size contributed to our finding. Treatment for hypotension is directed by SBP guidelines in our GSICU. Therefore, the treatment for hypotension was similar to the frequency of hypotension by SBP. In IHD run one and IHD run two, treatment occurred 36.4% of the time, respectively. In IHD run three, treatment for hypotension occurred 27.3% of the time. The overall percentage of treatment for all three IHD runs was 33%. This is lower than the occurrence for hypotension defined by both SBP <90 mmHg and MAP <70 mmHg. There is no consistent definition for hypotension in the ARF patient, thus degree of hypotension that affects recovery in the ARF patient needs to be determined.

Blood volume slopes. The most frequent BV slope was linear decrease for all IHD runs, thus it was also the most frequent BV slope occurring with hypotension. These findings differ from Andrulli et al.'s (2002), who found linear decrease to be the most common in patients who were normotensive, and concave upwards decrease to be the most common BV slope in hypotensive patients. There was no relationship found between BV slope and occurrence of hypotension in our cohort. Low inter-rater agreement for BV slope classification in all IHD runs may account for this finding.

Relationship of blood volume to blood pressure. BV was obtained at 15-minute intervals, and prior to hypotension, for each IHD run. BV monitoring devices depend on the fact that the blood components are confined to the vascular space enabling the measurement of relative blood volume. Therefore, as plasma water was removed by UF, the concentration of the blood compartment increased hematocrit (HCT) levels and there was a proportional decrease in circulating BV (Chamney et al., 1999). As expected, there was a decrease in BV as ultrafiltration occurred. Although there was a correlation between MAP, SBP and BV, this relationship was not significant. These findings were similar to Tonelli et al. (2002), who also found monitoring of BV could not predict episodes of forthcoming hypotension.

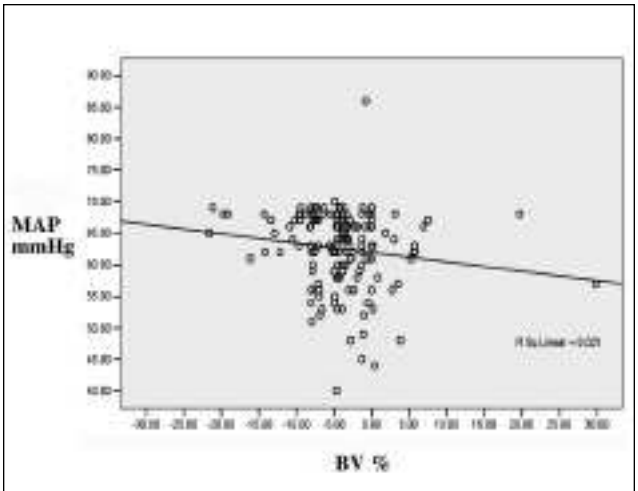

Figure Three: Relationship between Mean Arterial Pressure (MAP) and Critical Blood Volume (BV%)

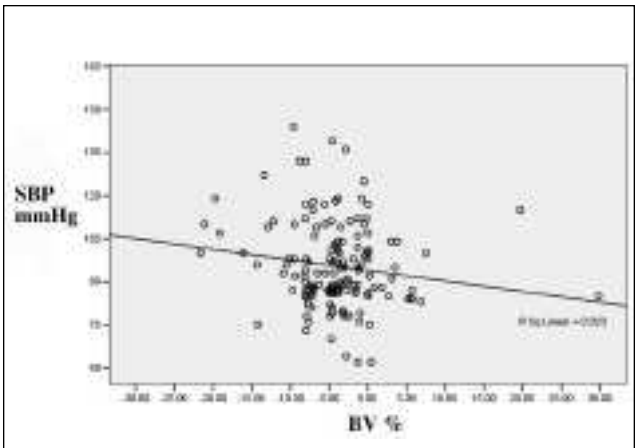

Figure Four: Relationship between Systolic Blood Pressure (SBP) and Critical Blood Volume (BV%)

Several factors may contribute to the inability of BV to predict forthcoming hypotension. Although hypovolemia contributes to hypotension in critically ill patients on IHD, there are other contributing factors as well. Other mechanisms such as autonomic dysfunction and abnormal vascular tone may affect plasma refill in the critically ill patient affecting the ability of BV monitoring to predict hypotension. We did not measure plasma refill with bioimpedance, which may have clarified whether abnormal vascular tone was contributing to abnormal plasma refill in the critically ill patient. Critical blood volume was calculated for all patients who experienced hypotension, however, we were unable to find a CBV for individual patients that could predict forthcoming hypotension. This may indicate that hypotension is more dependent on cardiovascular defense mechanisms such as sympathetic drive rather than on reduction in BV. Thus, CBV would not be able to consistently predict forthcoming hypotension, if hypotension is dependent on more than BV.

All patients were dialyzed through central venous catheters. It has been suggested that there is a difference in hematocrit levels between central blood and peripheral blood compartments (Tonelli et al., 2002; Prakash, Reddan, Heidenheim, Kianfar, & Lindsay, 2002), which, in turn, may affect the correlation of BV to hypotension. Another interesting element that was noted in this study was the high number of interdialytic alarms related to access pressures. This necessitates the blood pump speed be changed, which affects the accuracy of BV monitoring. Any time blood pump speeds are adjusted, BV monitoring needs to be recalibrated and does not resume until the pump speed is > 200 for five minutes. This may have affected the reliability of the monitoring device.

Limitations

The small sample size may have accounted for an inability to show a statistically significant relationship between BV and hypotension. The physicians and nurses in the GSICU were aware that hypotension in IHD was being evaluated, which could have led to modifications in treatment of patients on IHD. However, dialytic technique was standardized as much as possible during this study. The length of IHD runs and ultrafiltration removal rates varied between patients. However, this is usual in critical care practice when BV monitoring would be used. In this study, both arterial lines and automated sphygmomanometers were used to measure blood pressure, which may have introduced measurement error. In our cohort, all IHD runs were done via central venous catheters, as well, there were frequent access alarms that may have affected the reliability of the BV monitoring device. This may have accounted for our inability to determine a relationship between BV and hypotension in critically ill ARF patients in IHD. There is a need for further study to determine if a different monitoring device designed for use with central venous access could be used to predict hypotension.

Conclusions

Hypotension occurred in approximately 70% of all IHD runs for this cohort of critically ill ARF patients. Monitoring of BV was not shown to predict episodes of forthcoming hypotension. However, this does not preclude the need to implement strategies to reduce hypotension during dialysis. The multifactoral etiology of hypotension in ARF patients on IHD indicates that one simple strategy is unlikely to alleviate this problem. A group of critically ill patients who are older, have higher Apache scores, and have multiple comorbidities such as cardiac disease and diabetes mellitus with reduced cardiovascular defence mechanisms may be unable to compensate for a reduction in BV in order to prevent hypotension. This subgroup may benefit from less aggressive dialysis treatment strategies.

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Acknowledgements

We wish to acknowledge Dr. Marcello Tonelli for his invaluable contribution to the study design, data analysis, and review of findings. Financial and equipment support for the study was greatly received from Gambro, Canada, and the Canadian Association of Critical Care Nurses.

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