Effect of Dialysate Sodium Profiling and Gradient Ultrafiltration on Hypotension

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OBJECTIVE: This study aimed to investigate the effects of dialysate sodium profiling and gradient ultrafiltration on hypotension during hemodialysis.

METHODS: In this study, a single-blinded, crossover design of 4 different dialysis protocols was undertaken. Four hemodialysis protocols were administered to 40 patients to 2 mounts (12 hemodialysis sessions). A total of 40 patients experiencing hypotension episodes during hemodialysis and who agreed to participate were included in the study. All patients were administered 4 different hemodialysis protocols consecutively. Protocol 1 = linear sodium dialysate 1 (Na: 150 mEq/L and decreased by 4 mEq/L at each hour) and constant ultrafiltration; Protocol 2 = linear sodium dialysate and gradient ultrafiltration; Protocol 3 = constant sodium dialysate and gradient ultrafiltration; and Protocol 4 (standard hemodialysis) = constant sodium dialysate and constant ultrafiltration.

RESULTS: The results of this study show that when linear sodium dialysate and gradient ultrafiltration are used concomitantly, hypotension episodes decrease, more ultrafiltration is performed, and less treatment is needed. Gradient sodium dialysate usage (Protocol 1 and 2) required fewer treatment interventions for hypotension compared to standard protocol. No significant differences were observed between standard hemodialysis and any of the other protocols after dialysis for plasma osmolarity.

CONCLUSION: We recommend concomitant use of gradient ultrafiltration and sodium dialysate in patients with hypotension.

Hypotension is a common side effect of hemodialysis.[1] Intradialytic hypotension is a common adverse event that occurs in 20% to 50% of all dialysis treatments.[2,3] Dialysis hypotension usually presents in 1 of the 2 ways: as episodic hypotension (symptomatic hypotension), in which a sharp fall in blood pressure (usually late in dialysis) accompanied by signs and symptoms of hypotension are noted, and chronic persistent hypotension, in which systolic blood pressure is less than 90 to 100 mmHg at the onset of dialysis. Chronic persistent hypotension is estimated to occur in 3% to 5% of the dialysis population, whereas episodic hypotension occurs in between 15% and 25% of all dialysis encounters.[4] Chronic persistent hypotension is characterized by high circulating angiotensin II levels and maximal pre-dialysis vasoconstriction.[4,5] Symptomatic hypotension has multiple etiologies. Several studies have shown that a fall in plasma osmolality as ultrafiltration proceeds compounds extracellular volume depletion because fluid moves intracellularly.[6,7,8] This has led to the routine use of a higher sodium dialysate concentration with reported favorable outcomes.[9,10] Both of these conditions are therapeutic challenges because ultrafiltration requirements are difficult to achieve in the context of hemodynamic instability. Patients who are frequently hypotensive often feel unwell and spend the interdialytic period "recovering" from the preceding dialysis.[11]

Symptomatic hypotension can occur when the so-called dry weight of the patient is not attained. Dry weight cannot be determined exactly in hemodialysis. In practice, the choice of dry weight is most often based solely on clinical criteria.[12]

Dialysis hypotension has a multifactorial etiology, including such disparate causes as autonomic dysfunction,[13] decreased plasma osmolality,[6,14,15] a decrease in extracellular fluid volume with inadequate plasma,[5] decreased cardiac reserve,[16,17] impaired venous compliance,[18] and high plasma nitric oxide levels.[19] If there are no other reasons such as cardiac dysfunction or insufficiency of the autonomic nervous system, it is induced when ultrafiltration exceeds refilling of the intravascular compartment.[16,20]

Intradialytic hypotension associated with declining plasma osmolality due to diffusion contributes to complications that decrease patient's well-being during dialysis.[21,22] Many strategies have been devised to decrease osmolality change through intravenous mannitol,[7] gradient/ramping sodium dialysate,[15,21,23-25] ultrafiltration profiling,[26,27] and used with gradient sodium and gradient ultrafiltration.[7,9,22,28,29]

It has been shown that limiting the reduction in plasma osmolality during hemodialysis by selecting a higher sodium concentration of the dialysate improves ➲

hemodynamic stability. The disadvantage is that a higher dialysate sodium concentration increases the exchangeable sodium pool giving rise to increased interdialytic weight gain and hypertension.[12,30] This can be achieved by an increase in plasma osmolality and therapies of dialysis hypotension by using a higher sodium concentration in the dialysate. The potential dipsogenic effect of increased plasma osmolality can be minimized by using a gradient sodium program in which dialysate sodium is increased to 150 mEq/L during the first 3 hours and then decreased in a stepwise manner to 140 mEq/L for the last hour of the treatment.[22]

Sodium ramping is a technique in which a higher concentration of sodium than found in blood (usually between 150 and 160 mEq/L) is used in the dialysate early in dialysis, and this concentration is either continuously or in a stepwise manner decreased to approximately 140 mEq/L at the end of dialysis.[15]

Generally, the first response to intradialytic hypotension is to discontinue ultrafiltration and place the patient in the Trendelenburg position. The latter will increase cardiac filling by redistributing dependent vascular volume centrally and may increase blood pressure promptly. Commonly, however, a bolus of 100 mL of isotonic saline is administered to increase intravascular volume.[31]

The purpose of this study was to determine the effects of dialysate sodium profiling and gradient ultrafiltration on hypotension during hemodialysis.

Methods and Materials

A prospective and experimental design was used.

Sample

Among 90 chronic dialysis patients having dialysis for at least 6 months in a private dialysis center, 44 patients who had suffered frequent bouts of hypotension (at least 1 episode per hemodialysis session) during hemodialysis, without severe anemia (hematocrit <24%) or congestive heart failure and who agreed to participate were included in the study. Four patients withdraw from the study: 2 of them shifted to peritoneal dialysis, 1 had a renal transplant, and 1 developed vascular problems.

Of the remaining 40 patients, 30% were female. The mean age was 52.93 ± 12.42 years and the mean duration of dialysis was 28.48 ± 24.61 months.

Procedure

This study was approved by the Marmara University Medical Faculty Research Ethical Committee. Informed consent of hemodialysis patients meeting the study criteria was obtained.

All patients were given bicarbonate hemodialysis 3 times per week, each session being 4 hours, through a 1.5 m^2 cuprofan dialyser in an Altha Touch 2000 hemodialysis machine (Althin Medical, Ronneloy, Sweden). The temperature of the dialysate was kept constant at 36ºC and heparin (neuparin 5,000 U) was administered to provide anticoagulation.

In this study, a single-blinded, crossover design of 4 different dialysis protocols was undertaken. Four hemodialysis protocols were administered to 40 patients to 2 mounts (12 hemodialysis sessions). Each patient began the study by undergoing a standard dialysis (Protocol 4) with a sodium dialysate of 140 mEq/L. The patient underwent 12 hemodialysis sessions of standard dialysis. Following the completion of 12 hemodialysis sessions, each patient was then subjected to 2 mounts (12 dialysis sessions) of the 3 hemodialysis protocols performed respectively Protocol 1, Protocol 2, and Protocol 3.

In total, 1,920 hemodialysis sessions were evaluated. These protocols were as follows:

Protocol 1 = Linear sodium dialysate (150–138 mEq/L) and constant ultrafiltration

Protocol 2 = Linear sodium dialysate (150–138 mEq/L) and gradient ultrafiltration

Protocol 3 = Constant sodium dialysate (140 mEq/L) and gradient ultrafiltration

Protocol 4 (standard hemodialysis) = Constant sodium dialysate and constant ultrafiltration.

Linear Sodium Dialysate: Sodium dialysate was started during the first hour of the dialysis treatment at 150 mEq/L, than was decreased gradually, 4 mEq/L per hour until it was 138 mEq/L during the last hour of the dialysis.

Gradient Ultrafiltration: Two-thirds of the fluid acquired between 2 dialysis sessions were taken back during the first 2 hours of the dialysis treatment and the remaining one-third during the last 2 hours.

Constant Ultrafiltration: Excessive fluid acquired between hemodialysis was determined. This fluid was taken back in equal volumes at each hour of a 4-hour dialysis session.

Constant Sodium Dialysate: During a 4-hour dialysis session, sodium dialysate was kept at 140 mEq/L.

Data were collected on all hemodialysis during the mount. In each protocol, while serum glucose, sodium, blood urea nitrogen (BUN), hematocrit, and hemoglobin levels were measured before a monthly dialysis, serum glucose, sodium, and BUN levels were also measured after the dialysis.

Instrumentation

In each protocol, all patients had body weight measured and blood pressure was monitored at 30-minute intervals during dialysis. Blood pressure was measured every 30 minutes from the arm without fistula with a cuff mounted sphygmomanometer with Korotkoff sounds taken into consideration. Hypotension was defined as diastolic blood pressure lower than 90 mmHg or a 20% decrease from the previous value. Nursing interventions for hypotension were recorded. Patients with hypotension or the symptoms of hypotension, such as nausea/vomiting, vertigo, and fatigue/malaise were primarily given position (feet elevated to 45º). Ultrafiltration was interrupted if symptoms did not improve and hypotension persisted. Ultrafiltration was restarted if symptoms improved and blood pressure returned to normal. A solution of 100 mL of 0.9% NaCl (normal saline) was infused if hypotension and symptoms persisted despite positioning and stopping ultrafiltration. Ultrafiltration was discontinued until the end of the treatment if hypotension and symptoms still did not improve (early termination of dialysis). If despite all these interventions the hypotension attack did not improve, the treatment was terminated and the physician informed.

TABLE I. Comparison of standard HD and the other three protocols according to mean systolic blood pressure levels (n = 40).

Protocols	Before HD SBP (mmHg) Mean ± SD	Hour 1 SBP (mmHg) Mean ± SD	Hour 2 SBP (mmHg) Mean ± SD	Hour 3 SBP (mmHg) Mean ± SD	Hour 4 SBP (mmHg) Mean ± SD
Standard HD	135.00 ± 16.33	125.50 ± 16.01	119.75 ± 18.74	113.25 ± 19.27	119.50 ± 17.70
Protocol 1	133.25 ± 17.60	125.50 ± 16.79	121.50 ± 16.72	114.00 ± 17.37	119.00 ± 16.50
t and p	1.226 0.227	0.00 1.000	−1.069 0.291	−0.368 0.715	0.313 0.756
Standard HD	135.00 ± 16.33	125.50 ± 16.01	119.75 ± 18.74	113.25 ± 19.27	119.50 ± 17.70
Protocol 2	134.00 ± 18.65	123.25 ± 16.85	117.75 ± 18.33	112.00 ± 18.56	117.75 ± 17.50
t and p	0.726 0.472	1.548 0.130	1.537 0.132	0.710 0.482	1.096 0.280
Standard HD	135.00 ± 16.33	125.50 ± 16.01	119.75 ± 18.74	113.25 ± 19.27	119.50 ± 17.70
Protocol 3	132.50 ± 17.51	121.50 ± 17.48	113.00 ± 17.28	109.50 ± 17.82	117.00 ± 17.42
t and p	1.818 0.077	3.122 0.003[b]	4.970 0.000[c]	2.423 0.020[a]	1.883 0.067

Abbreviations: DBP, diastolic blood pressure; HD, hemodialysis; SBP, systolic blood pressure.
Note: [a]p < 0.05, [b]p < 0.01, [c]p < 0.001.

TABLE II. Comparison of standard HD and the other three protocols according to mean diastolic blood pressure levels (*n* = 40).

Protocols	Before HD DBP (mmHg) Mean ± SD	Hour 1 DPB (mmHg) Mean ± SD	Hour 2 DBP (mmHg) Mean ± SD	Hour 3 DBP (mmHg) Mean ± SD	Hour 4 DBP (mmHg) Mean ± SD
Standard HD	79.50 ± 7.83	76.75 ± 6.94	74.25 ± 8.13	71.25 ± 9.11	75.00 ± 7.51
Protocol 1	78.75 ± 5.63	76.75 ± 6.56	75.25 ± 7.84	72.00 ± 8.83	74.75 ± 7.16
t and *p*	0.723 0.474	0.000 1.000	1.071 0.291	0.723 0.474	0.374 0.711
Standard HD	79.50 ± 7.83	76.75 ± 6.94	74.25 ± 8.13	71.25 ± 9.11	75.00 ± 7.51
Protocol 2	78.75 ± 7.23	77.00 ± 7.23	74.75 ± 7.84	71.75 ± 8.13	74.25 ± 8.44
t and *p*	0.684 0.498	0.330 0.743	0.495 0.623	0.572 0.570	1.000 0.323
Standard HD	79.50 ± 7.83	76.75 ± 6.94	74.25 ± 8.13	71.25 ± 9.11	75.00 ± 7.51
Protocol 3	79.00 ± 7.44	75.50 ± 6.78	71.25 ± 9.10	69.50 ± 9.86	74.00 ± 7.44
t and *p*	0.495 0.623	1.706 0.096	3.122 0.003[b]	2.211 0.033[a]	1.160 0.253

Note: [a]p < 0.05, [b]p < 0.01.

Statistical Analysis

The study data were analyzed using Statistical Package for Social Sciences program (SPSS version 11); descriptive statistics were expressed as frequencies, percentages, and means ± SDs. A Student's *t*-test was used to test differences of blood pressure, ultrafiltration, plasma osmolarity, sodium, and BUN between protocols and a McNeamer test was used to test differences between hypotension attacks.

Results

Compared to standard hemodialysis, hourly systolic blood pressures at 1, 2, and 3 hours decreased more with Protocol 3, and hourly diastolic blood pressures at 2 and 3 hours decreased more with Protocol 3 (*Tables I* and *II*). Compared to standard hemodialysis, blood pressure decreased more with Protocol 3.

All hypotension episodes which occurred were recorded in each hemodialysis session. The number of patients experiencing hypotension was 18 at Protocol 1, 10 at Protocol 2, 32 at Protocol 3, and 26 at Protocol 4. According to the number of patients experiencing hypotension, while there was no significant differences between standard hemodialysis and Protocol 1 ($\chi^2 = 4.0$, $p = 0.77$) and Protocol 3 ($\chi^2 = 3.0$, $p = 0.146$), there was significant difference between standard hemodialysis and Protocol 2 ($\chi^2=12.80$, $p = 0.000$). The number of patients ➲

TABLE III. Comparison of standard HD and the other three protocols according to pre-dialysis and post-dialysis blood biochemistry parameters (n = 40).

Blood Biochemistry Parameters	Protocol 1 Mean ± SD	Protocol 2 Mean ± SD	Protocol 3 Mean ± SD	Standard HD Mean ± SD	Standard HD and Protocol 1 *t* and *p*	Standard HD and Protocol 2 *t* and *p*	Standard HD and Protocol 3 *t* and *p*
B-HD Na^+ (mEq/L)	137.73 ± 2.4	138.50 ± 1.6	138.30 ± 2.2	139.28 ± 2.2	3.200 0.003[b]	1.925 0.062	2.895 0.006[b]
A-HD Na^+ (mEq/L)	138.88 ± 1.4	138.63 ± 1.0	138.93 ± 1.6	139.32 ± 1.4	1.433 0.160	2.759 0.009[b]	1.292 0.204
B-HD BUN (mg/dL)	67.60 ± 11.174	69.00 ± 9.69	67.55 ± 9.90	65.93 ± 8.90	1.075 0.289	2.043 0.048[a]	1.057 0.297
A-HD BUN (mg/dL)	22.25 ± 6.15	21.35 ± 5.54	20.38 ± 5.66	18.85 ± 5.17	4.400 0.000[c]	2.764 0.009[b]	2.217 0.033[a]
B-HD Plasma Osm	306.10 ± 5.26	307.55 ± 5.67	308.30 ± 5.92	309.30 ± 6.81	2.732 0.009[b]	1.501 0.141	1.168 0.250
A-HD Plasma Osm	291.13 ± 4.05	291.30 ± 3.92	291.85 ± 4.62	291.83 ± 4.71	0.851 0.400	0.677 0.502	0.30 0.976

Abbreviations: A-HD, after hemodialysis; B-HD, before hemodialysis; BUN, blood urea nitrogen; Osm, osmolarity.
Note: [a]p < 0.05, [b]p < 0.01, [c]p < 0.001.

experiencing hypotension was fewer with Protocol 2 than standard hemodialysis.

The amount of ultrafiltration was 2.8 L (SD = 0.6) in Protocol 1, 2.8 L (SD = 0.6) in Protocol 2, 2.6 L (SD =0.6) in Protocol 3, and 2.6 L (SD = 0.6) in Protocol 4. There were significant differences for the amount of ultrafiltration between standard hemodialysis and Protocol 1 (t =2.247, p = 0.030) and Protocol 2 (t =2.342, p = 0.024), but there were no such differences between standard hemodialysis and Protocol 3 (t = 0.000, p = 1.000).

Differences between standard hemodialysis and the other 3 protocols according to BUN, serum, sodium, and plasma osmolarity levels in before and after dialysis were reported in *Table III*.

The treatment for hypotension and the need for positioning was not significantly different with Protocol 3 than standard hemodialysis (χ^2 = 1.600, p =0.344) although with Protocol 1 and Protocol 2 the differences were significant (χ^2 = 6.250, p = 0.021; χ^2 = 15.210, p = 0.000). Fewer patients needed positional change due to hypotension with Protocol 1 and Protocol 2 than standard hemodialysis.

While there was no difference between standard hemodialysis and Protocol 3 for 100 mL saline infusion (χ^2 =3.769, p = 0.092), there were significant differences between standard hemodialysis and either Protocol 1 (χ^2 = 6.230, p = 0.022) or Protocol 2 (χ^2 = 5.400, p = 0.035). Fewer patients needed saline infusion due to hypotension with Protocol 1 and Protocol 2.

There were no significant differences between standard hemodialysis and Protocol 1 (χ^2 = 0.888, p =0.625), Protocol 2 (χ^2 = 4.764, p = 0.375), and Protocol 3 (χ^2 = 3.769, p = 0.250) for the cessation of hemodialysis due to hypotension. There were no early hemodialysis terminations due to hypotension in any of the protocols.

Discussion

In this study, there were no significant differences for hourly systolic and diastolic blood pressure levels with Protocol 2 where linear sodium dialysate and gradient ultrafiltration are used concomitantly although hypotension episodes diminished. This finding is similar to those of some other studies.[15,22] Meers et al used the sodium dialysate of 150 mEq/L for 3 hours, stepping down to 140 mEq/L for the last hour of the dialysis (gradient sodium dialysate).[22] In Sang et al's study, linear and gradient sodium dialysate protocols caused markedly less hypotension compared to standard hemodialysis and the lowest blood pressure levels were observed with standard hemodialysis.[15] Dumler et al, using different sodium dialysate and ultrafiltration, observed a relative but statistically insignificant decrease in the number of hypotension.[28]

Takenaka et al compared standard dialysate and high sodium dialysate (during the first 2 hours, 150 mEq/L, than during the last 2 hours, 140 mEq/L) and evaluated blood pressure levels.[24] They reported that with high sodium dialysate, hypotension was prevented. Ahbap also reported significant decrease in hypotension when a constant ultrafiltration and a high sodium dialysate, starting with a sodium level of 150 mEq/L and decreasing 5 mEq/L per hour till it reaches 135 mEq/L over the last hour of the dialysis was used and compared to standard hemodialysis.[25] Our results with Protocol 2 are concordant with Ahbap's and Takenaka et al's findings.[24,25]

In our study, Protocol 3 provided significantly higher decreases in systolic and diastolic blood pressures compared to standard hemodialysis although no such difference was observed for the number of hypotension episodes. Thus, our results suggest that dialysis with gradient ultrafiltration may result in higher decrease in blood pressure. Dheenan and Henrich found a significant increase in hypotension episodes with a standard hemodialysis and ultrafiltration model.[7] They reported that increased symptoms with the ultrafiltration model were due to the increase in the number of ultrafiltrations in a shorter period. Compared with standard hemodialysis, they reported significantly fewer hypotension episodes with high sodium dialysate.

The effect of plasma osmolarity on blood pressure could not be shown with all protocols. At the end of dialysis, the difference in sodium but not plasma osmolarity was found to be significant with Protocol 2 compared with standard hemodialysis. Henrich et al investigated the role of osmolarity on blood pressure equilibrium during ultrafiltration and after dialysis using 5 different hemodialysis protocols.[6] At the end of the second hour, protocols using isolated ultrafiltration and hypertonic mannitol 20% were the ones with the highest plasma

osmolality. Patients in the low osmolality treatment group showed hypotension symptoms upon standing.

In this study, Protocol 1 and 2 allowed more ultrafiltration and required fewer treatment interventions for hypotension, such as positioning or isotonic solution infusion. On the other hand, Protocol 3 allowed less ultrafiltration but required more treatment. Since there was not any difference in terms of exit plasma sodium, osmolarity, and ultrafiltration between standard hemodialysis and Protocol 3, no difference related to the occurrence of hypotension was expected. Meers et al reported a significant decrease in all kinds of treatment for hypotension in all protocols with gradient dialysate and gradient ultrafiltration.[22] It was observed that in protocols using a high dialysate, the amount of liquid received between dialysis, thus the need for ultrafiltration, was higher.[15,25,27] Ahbap reported significantly higher number of treatments for hypotension with standard protocol compared to high sodium dialysate protocols.[25] These results are comparable to our findings. Gradient sodium dialysate usage (Protocols 1 and 2) required fewer treatment interventions for hypotension compared to standard protocol. We recommend concomitant use of gradient ultrafiltration and sodium dialysate in patients with hypotension.

Limitations

Due to sample size problems, this study's findings may not be generalized to all hemodialysis patients. Larger studies evaluating gradient sodium protocols and hourly plasma osmolarity are needed.

Conclusion

The results of this study show that when linear sodium dialysate and gradient ultrafiltration are used concomitantly, frequency of hypotension decreases, more ultrafiltration is performed, and fewer treatment interventions are needed, although no significant difference was found in hourly systolic and diastolic blood pressure levels. These results have important implications for studies in the hemodialysis field, which are scarce in number. The decrease in the number of hypotension attacks during dialysis allows more time for the nurse and helps the patient to go through a more comfortable dialysis.

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