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Original Article

Prevention of hemodynamic instability during hemodialysis in cardiac-compromised hypotension-prone patients

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Abstract

Background. Hypotension is the most common complication of hemodialysis (HD). The aim of this study was to investigate the efficacy of hypertonic saline (10%), albumin (20%), and 10% hydroxyethylstarch (HES) on blood pressure (BP) course during HD session in cardiac-compromised hypotension-prone HD patients.
Methods. Fifteen patients (8 female, 7 male), age ranging from 56-80 years, undergoing chronic HD for 6-36 months, were included in the investigation. All patients were cardiac-compromised (NYHA III-IV), with ejection fraction ranging from 23-40%. Intra-dialytic hypotension was experienced in all patients more than once a week. Dry body weight was estimated on clinical basis. The patients were studied during three HD sessions that differed only in the type of intravenous fluid administered. In the randomized order, an intravenous infusion of 12 ml of saline (10 % sodium chloride), 100 ml of albumin (20%) or 100 ml of HES (10%) was administered when systolic blood pressure (SBP) was less than 90 mmHg, or when the SBP decreased more than 30 mmHg.
Results. Systolic BP decreased significantly versus baseline during HD in all three sessions ($p<0.05$). The decrease was significantly greater when using saline compared with albumin ($p<0.05$) or with HES ($p<0.05$). There was no significant difference in SBP decrease between the patients treated with albumin and those treated with HES. Diastolic BP decreased significantly versus baseline during HD and treatment with saline and albumin ($P<0.05$) but not with HES. Diastolic BP at the end compared to DBP at the start of HD session decreased with saline, increased with albumin, and increased significantly with HES. There was no significant difference in inter-dialytic weight gain after the treatment with hypertonic saline, albumin or HES. Three patients experienced a hypotensive episode when using saline and one patient experienced a hypotensive episode when using albumin. However, ultrafiltration could be continued when the patients were placed in the Trendelenburg position.
Conclusion. Our results demonstrate that SBP was better maintained with albumin (20%) or HES, compared with hypertonic saline. The increase in SBP was greater with HES compared to albumin. It is possible that higher sodium concentration of HES has an additional beneficial effect on the SBP course, without repercussion on the inter-dialytic weight gain.

Keywords: hemodialysis; intra-dialytic hypotension; treatment; prevention; saline; HES; albumin; heart failure

Introduction

Intra-dialytic hypotension (IDH) is the most common complication of hemodialysis (HD) that may induce minor side effects such as dizziness, muscle cramps, nausea, and vomiting, but may also lead to more serious complications, such as subendocardial ischemia, severe arrhythmias or neurological complications [1,2]. Dialysis-associated hypotension is especially frequent in elderly patients and in those with compromised cardiovascular system [3-6].
Pathophysiology and treatment of IDH have been extensively studied, and most of the papers emphasized its multifactorial origin [3,7,8]. The immediate cause of hypotension is reduction of intravascular volume that is most frequently treated by injecting hypertonic saline [9]. However, because of side effects of the hypertonic saline (hypertension, thirst, and inter-dialytic weight gain) this therapy is not without drawbacks. Volume expansion can also be achieved by hyperoncotic infusions, such as dextran and mannitol [10,11], but their use is of limited clinical importance because of side effects [9-13]. An intravenous infusion of albumin or other hyperoncotic fluids further enhance vascular refilling and could improve hemodynamic stability [14]. Recently, an increased risk of death was reported in critically ill patients treated with albumin [15]. Data on the effect of hypertonic saline,

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hydroxyethylstarch (HES) and albumin on systolic blood pressure (SBP) course in cardiac-compromised HD patients with frequent hypotensive episodes are scarce.
The aim of this study was to investigate the efficacy of hypertonic saline (10%), albumin (20%), and HES (10%) on the blood pressure (BP) course during combined ultrafiltration (UF) and HD in cardiac-compromised HD patients.

Patients and methods

Study Population and Dialysis

Fifteen patients (8 female and 7 male) undergoing chronic, intermittent HD, were included in the investigation. All patients were cardiac-compromised (New York Hearth Association /NYHA/ classification III-IV) [16], and had a mild-to-severe left ventricular dysfunction (ejection fraction /EF/ of 40% or less), which was determined by the two-dimensional echocardiogram after HD. All the patients experienced IDH more than once a week. Informed consent was provided by all participants. The study was approved by the Sestre Milosrdnice University Hospital Ethics Committee.
Dry body weight (DBW) was determined clinically by the nephrologist. The UF rate was prescribed according to the estimated DBW and inter-dialytic weight gain, and was constant during a single HD session. Hemodialyses were performed using the Nipro NCU 10E modules (Nissho Nipro Corporation, Japan) with hollow fiber dialyzers (hemophane membrane - Hospal, France; cellulose diacetate membrane - Pliva, Croatia). The blood flow ranged from 220 to 280 ml/min, with the dialysate flow of 500 ml/min. The dialysate concentrate (H-K DM 10 and H-K 6, Pliva, Croatia) composition was as follows: sodium 100 mmol/L, potassium 2 mmol/L, calcium 1.5-1.75 mmol/L, magnesium 0.375 mmol/L, chloride 105.75 mmol/L, acetate 2 mmol/L. The dialysate bicarbonate concentration was individualized and adjusted to achieve a post-dialysis serum bicarbonate level between 26 and 30 mmol/L. The dialysate temperature was adjusted to the patient's pre-dialysis body temperature. The dialysate temperature and dialysate composition did not differ between the three treatment sessions.

Study Protocol

The ESRD patients were studied on the days of their regular dialysis. Each patient served as his or her own control and was studied during three sessions that differed only in the type of intravenous fluid administered. The study started with the insertion of needles with patient in the supine position during the dialysis session.
Intravenous infusion of 12 ml of saline (10% sodium chloride; Croatian Institute for Transfusion Medicine, Zagreb, Croatia), 100 ml of albumin (20% human albumin; Institute of Immunology, Zagreb, Croatia), or 100 ml of HES (10% HAES-steril; Fresenius, Bad Homburg, Germany) was administered at room temperature (22°C) when SBP was less than 90 mm Hg, or when it decreased more than 30 mm Hg in relation to the start of UF and HD, in which case UF was continued at the same rate. The osmolar load of the administered saline (309 mosm/L) was similar to the osmolar load of HES (308 mosm/L). The order of the intravenous infusions was randomized. Measurements of arterial BP were performed just before the start of UF and HD (t=0), when SBP was less than 90 mm Hg or when the decrease in SBP was more than 30 mm Hg versus the start of UF and HD (t=iv); after one (t=1), 5 (t=5), and 30 (t=30) min after t=iv; and at the end of UF and HD (t=end).

Measurements and Laboratory Methods

Blood pressure (SBP, and diastolic BP /DBP/) was measured every 30 minutes routinely and every 10-15 minutes if the patient became symptomatic or if BP decreased. Moreover, SBP and DBP were also measured at t=iv, t=1, t=5, t=30, and t=end.
Before and at the end of HD, the blood sample was taken to determine the levels of serum sodium and ionized calcium (Chiron Diagnostics, Essex, UK), blood urea nitrogen and creatinine (Beckman CX-/, Brea, USA).

Dialysis Adequacy

Dialysis adequacy (Kt/V) in HD patients was calculated using the second-generation formula introduced by Daugirdas [17]. Blood samples for determinations of urea were taken before and immediately after HD.

Statistical Analysis

All values are expressed as mean ± SD. The parameters assessed during different treatments were analyzed with paired Student's t-test and ANOVA. P value lower than 0.05 was considered significant.

Results

Patient Characteristics

The mean patient age was 70.4 years (range, 56-80 years), and the mean time on HD was 22.1 months (range, 6-36 months). End-stage renal disease was caused by benign nephrosclerosis (7 patients), chronic glomerulonephritis (3 patients), diabetic nephropathy (3 patients), and chronic pyelonephritis (2 patients). The mean residual diuresis was 185 ml (range: 0 to 840 ml/day). Heart failure resulted from one or more myocardial infarctions (6 patients), ischemic heart disease (3 patients), left ventricular systolic dysfunction (4 patients), and dilated cardiomyopathy (2 patients). The mean EF of the patients was 28.7±8.4% (range, 23 to 40%).
The pre-dialysis DBW in the three study treatment sessions (saline, albumin, and HES) were 67.5±12.82, 66.9±12.63, and 66.74±12.69 kg, respectively. The UF rate was 0.92±0.31, 0.86±0.39, and 0.91±0.25 L/h in the three treatment sessions. The differences were not statistically significant. The mean Kt/V was 1.16±0.6, and did not significantly changing during HD sessions. The

dialysate temperature during all three HD sessions was 36.93±0.39°C.

Changes in Blood Pressure

Table 1 shows the SBP during HD sessions in hypotension-prone patients treated with three different hypertonic solutions. There were no statistically significant differences in duration of intravenous infusion of saline, albumin, and HES (147±67, 144±58, and 150±76 min, respectively). Systolic BP decreased significantly versus baseline (t=0) during UF and HD in all three treatment sessions ($p<0.05$). The decrease was significantly higher when using saline compared with albumin ($p<0.05$) and when using saline compared with HES ($p<0.05$). There were no significant differences between albumin and HES.

When the values at t=iv with those at t=end were compared, SBP decreased with saline (change in SBP, -8.71±16.63 mmHg; NS), increased with albumin (change in SBP, +8.66±16.61 mmHg; NS), and increased significantly with HES (change in SBP, +16.11±19.37 mmHg; $p<0.05$). The change in SBP at t=end versus t=iv was significantly greater when using saline compared with HES ($p<0.05$) and tended to decrease more when using saline compared with albumin ($p=0.09$). There were no significant differences between albumin and HES.

Table 1. Systolic SBP course during treatment with three different solutions

Variable SBP (mmHg)	Saline (10%)	Albumin (20%)	HES (10%)
t=0	128.1±60.6	122.3±58.2	128.2±62.0
t=iv	84.8±40.0	81.0±38.6	82.3±40.2
t=5	99.3±47.0	96.2±45.5	96.3±45.5
t=15	99.3±46.5*	106.9±50.3	105.6±49.6
t=30	96.8±45.4*	105.6±49.6	103.0±48.1
t=60	90.9±42.5*	100.8±49.6	98.8±46.0
t=end	93.4±35.3*#	98.8±36.9#	100.3±37.2#

* $p<0.05$ vs. albumin and HES, # $p<0.05$ vs. t=0

Diastolic BP decreased significantly versus baseline (t=0) during UF and HD with saline and albumin ($p<0.05$), but not with HES. When the values at t=iv with those at t=end were compared, DBP decreased with saline (change in DBP, -5.71±16.70 mmHg; NS), increased with albumin (change in DBP, +2.89±10.05 mmHg; NS), and increased significantly with HES (change in DBP, +7.55±10.38 mmHg; $p<0.05$). The change in DBP at t=end versus t=iv tended to decrease more when using saline compared with HES ($p=0.075$) (Table 2). There were no significant differences between albumin and HES and between albumin and saline.

Table 2. Diastolic BP course during treatment with three different solutions

Variable DBP (mmHg)	Saline (10%)	Albumin (20%)	HES (10%)
t=0	67.7±9.3	65.5±6.0	66.7±5.9
t=iv	59.3±7.5	57.3±6.9	57.9±6.4
t=5	64.8±5.6	67.1±5.3	66.5±5.1
t=15	61.6±6.7*	67.2±4.7	65.3±5.1
t=30	57.7±5.8*	62.9±4.6	62.3±4.9
t=60	58.1±7.0	58.9±5.1	60.1±5.1
t=end	56.5±7.3&#	57.3±5.7&#	60.0±4.8#

*$p<0.05$ vs. albumin and HES, & $p<0.05$ vs. HES, # $p<0.05$ vs. t=0

Table 3. Laboratory data before the start of HD and at the end of the HD session

Laboratory data	Saline (10%)		Albumine (20%)		HES (10%)	
	t=0	t=end	t=0	t=end	t=0	t=end
Creatinine (umol/L)	1010±213.4[a]	401.1±113.3*	1041.6±217.6	421.4±100.7*	1058.7±220.7	423.6±98.2*
Urea (mmol/L)	29.3±3.9	7.9±1.1*	29.8±3.4	8.4±0.9*	29.2±3.4	7.9±0.8*
Sodium (mmol/L)	138.5±2.0	136.0±2.0*	135.8±2.2	136.9±1.5	136.8±1.8	135.9±1.6*
Calcium (mmol/L)	1.24±0.04	1.31±0.02*	1.27±0.03	1.31±0.03*	1.27±0.03	1.34±0.02*

* $p<0.001$ vs. t=0, [a] $p<0.05$ vs. albumine and HES

The inter-dialytic weight gain after treatment sessions with saline, albumin, and HES was 2.63±0.38, 2.43±0.34, and 2.63±0.71 kg, respectively, with no significant difference between the three treatment sessions. Three patients experienced a hypotensive episode when using saline and one patient experienced a hypotensive episode when using albumin. However, UF could be continued when the patients were placed in the Trendelenburg position.

The laboratory data are presented in Table 3. The change in serum sodium was comparable between the three treatment sessions. During all sessions there was a significant increase in ionized calcium and decrease in BUN. There were no significant differences in change in ionized calcium and BUN between the sessions.

Discussion

Intra-dialytic hypotension is common, occurring in 20 to 30% of HD sessions [1,3,18,19]. The adequacy of intradialytic sodium and water removal plays a pivotal role in preventing both IDH and overhydration. It had been assumed that the primary cause of IDH was induction or exacerbation of intravascular volume depletion by rapid UF. This hypothesis was disproved by the observation by Bergstrom *et al*. [20] that patients who became hypotensive during HD tolerated the same degree and rate of fluid removal with pure hemofiltration with no diffusive component of solute loss. During conventional HD, the rapid diffusive removal of urea and other small solutes results in a reduction of plasma osmolality, which shifts water into the cells, further depleting the extracellular volume, which has also diminished by UF. It is also possible that the rapid fall in plasma osmolality contributes to the hemodynamic instability, perhaps by interfering with symphatetic responsiveness to the volume depletion [21]. On the contrary, isolated UF does not create the osmotic gradient between the cells and the extracellular fluid, while the removed fluid has the same concentration of small solutes as the plasma. The fall in intravascular volume will raise the plasma protein concentration and therefore the plasma oncotic pressure, drawing water from the extracellular space and the cells into the vascular space, thereby leading to the relative preservation of intravascular volume [22,23].

It has been shown that limiting the reduction in extracellular osomolality by injecting hypertonic fluids could be an efficient treatment of symptomatic hypotension [6]. However, repeated intravenous injections of saline may lead to an increase in the exchangeable sodium pool and, as a consequence of thirst, may lead to an increase in inter-dialytic weight gain and hypertension, which may be of great clinical importance in cardiac-compromised dialysis patients [24,25]. In the present study two hypertonic fluids (HES, 10%, which is also a hyperoncotic fluid), and saline (10%) were compared with albumin (20%), a hyperoncotic fluid with an osmolality between 260 and 280 mosm/L, with respect to their effect on SBP. Saline and HES were administered in such amounts that a similar osmolar load was given. It was found that SBP was better maintained with HES compared with saline, suggesting that it is not only the effect of osmolality, but also the additional oncotic effect of HES that is responsible for the distinct and prolonged effect on SBP course.

It can be expected that hypertonic HES (10%) may be of even greater clinical importance in cardiac-compromised HD patients who often experience IDH. Van der Sande *et al*. [26] have evaluated the effect of normal saline, 20% albumin, or HES on preservation of blood volume in HD patients [26]. There was no significant difference in SBP among the three groups, but the preservation of blood volume was significantly better with HES and albumin compared with saline [26]. However, the increase in SBP, although not significant, was greater with HES compared to albumin [26]. It is possible that the higher sodium concentration of HES compared to albumin has an additional beneficial effect on SBP. In their second study, van der Sande *et al.* [27] investigated the effect of hypertonic (3%) saline, 20% albumin, and 10% HES in dialysis patients with frequent hypotensive episodes. Systolic BP was better maintained with HES or albumin, compared with saline [27]. The increase in SBP, although not significant, was greater with HES compared to albumin. Similar osmotic load of HES and saline indicate the responsibility of additional oncotic effect of HES on SBP course. In a randomized, blinded, crossover clinical trial, Knoll *et al*. [28] evaluated the effect of normal saline and 5% albumine in the treatment of IDH in 72 chronic HD patients. The percentage of target UF achieved was 0.84 ± 0.17 for 5% albumin compared with 0.80 ± 0.16 for saline. The post-dialysis SBP, postdialysis DBP, volume of study fluid used to treat IDH, time required to restore the BP, total nursing time required to manage the hypotensive episode, number of treatment failures (22% *vs.* 24%), and the frequency of recurrent IDH (36% *vs.* 36%) were not significantly different when 5% albumin was used compared with saline. It is concluded that 5% albumin is no more effective than normal saline for the initial fluid treatment of IDH in chronic HD patients [28]. Gong *et al.* [29] compared hypertonic saline solutions with dextran, which also has oncotic effects, and found that SBP response was more prolonged with 23% saturated hypertonic saline and dextran compared with hypertonic saline alone (7.5%). However, the majority of patients needed repeated intravenous infusions to maintain SBP [29]. Nette *et al*. [30] compared the effect of no infusion with isovolumetric infusion of isotonic and 3% saline, isotonic and 20% glucose, and 20% mannitol, in 6 patients during the first hour of 6 standardized HD sessions with UF. The maximum increase in relative blood volume (RBV) directly after infusion was significantly greater with 20% glucose than with all other infusions. Stroke volume increased and total peripheral resistance decreased significantly after hypertonic glucose infusions. As mannitol has the same osmolarity, molecule mass and charge, the greater increase in RBV following hypertonic glucose appears to be a specific effect, possibly related to a decline in vascular tone. It is therefore uncertain whether the observed increase in

plasma volume during hypertonic glucose infusions will be of clinical benefit [30].

In the present study SBP was better maintained with albumin compared with hypertonic saline, which could be caused by the oncotic effects of albumin. These data are also comparable with the results of previous studies, in which it has been found that SBP, although not significantly, was better maintained with albumin compared to saline [2,26,27]. The effect of HES on BP control was not significantly different when compared to that of albumin. The increase in SBP, although nor significant, was greater with HES compared to albumin. It cannot be excluded that the higher sodium concentration of HES has an additional beneficial effect on SBP course. This difference in sodium concentration does not appear to introduce untoward clinical effects, because the change in serum sodium during HD and interdialytic weight gain during the days after treatment were comparable between the three sessions.

By applying conductivity kinetic model to ESRD patients prone to IDH, Locatelli *et al*. [4] observed a significantly lower reduction in intra-dialytic SBP, and trend toward a reduction in symptomatic IDH, without modifying the dialysate and reinfusate sodium concentration values, or patient's DBW [4]. More recent investigations have suggested that the disparate hemodynamic responses to fluid and solute removal during HD and hemofiltration may be dissociated from changes in osmolality, membrane bioincompatibility, pyrogen-containing dialysate, thermal stress, catecholamine and other vasoactive hormones release, or venous tone [21,31-33]. In order to evaluate the safety, efficacy, and cost of treatment of HD-associated hypotension, Emili *et al*. [34] designed a protocol consisting of the stepwise use of saline, mannitol, and albumin. The protocol was evaluated prospectively in 2559 consecutive HD sessions in a total of 442 patients. Hypotension occurred during 24% of sessions, and reversal of low BP was achieved without the need for albumin in 91% of cases [34]. From these data, data from recently published studies [26,27], and from the authors' results, it is concluded that HES (10%) is an effective solution for maintaining BP in hypotensive-prone HD patients, comparable to albumin (20%), but superior to hypertonic saline. Given the side effects and cost of albumin, HES may be preferred [35].

An integrated approach to HD-associated hypotension would consist of the prevention of reduction in SBP or a symptomatic fall in mean BP by preserving plasma volume (the assessment of an optimal fluid state (DBW), minimizing interdialytic weight gain, sodium modeling, individualizing UF targets), optimizing the cardiovascular function (avoiding food ingestion before and during HD, avoiding acetate containing dialysate, increasing calcium concentrate of dialysate, reducing dialysate temperature, using sequential UF followed by isovolemic HD or HF, using biocompatible dialyser membranes), and finally, by a protocol-based response if IDH could not be prevented. Perhaps the greatest promise in minimizing this complication lies in technologies capable of adjusting of the dialysate composition and rate of UF continuously throughout the procedure on the basis of real-time changes in parameters that influence vascular refilling. The delivery of HD in this manner allows for adjustments to be made on the basis of minute-to-minute variations in the response of the cardiovascular system to UF.

Conflict of interest statement. None declared.

References

1. Zucchelli P, Santoro A *et al*. Dialysis-induced hypotension: a fresh look at patophysiology. *Blood Purif* 1993; 11: 981-5.
2. Laupacis A, Muirhead N, Keown P, Wong C. A disease-specific questionnaire for assessing quality of life in patients on hemodialysis. *Nephron* 1992; 60: 302-6.
3. Henderson LW *et al*. Hemodynamic instability during hemodialysis. *Kidney Int* 1986; 30: 605-12.
4. Locatelli F, Andrulli D, Di Filippo S *et al*. Effect of on-line conductivity plasma ultrafiltrate kinetic modeling on cardiovascular stability of hemodialysis patients. *Kidney Int* 1998; 53: 1052-60.
5. Kes P, Drusko D, Rupcic V *et al*. Cardiovascular complications in end-stage renal disease and hemodialysis patients. *Acta Med Croat* 1996; 50: 199-208.
6. Leunissen KLM, Kooman JP, van Kuijk WHM, Luik AJ, van der Sande FM, van Hooff JP. Preventing hemodynamic instability in patients at risk for intradialytic hypotension. *Nephrol Dial Transplant* 1996; 1(Suppl 2): 11-5.
7. Campese VM *et al*. Cardiovascular instability during hemodialysis. *Kidney Int* 1988; 33(Suppl 24): 186-90.
8. De Simone G *et al*. Left ventricular geometry and hypotension in end-stage renal disease: a mechanical perspective. *J Am Soc Nephrol* 2003; 14: 2421-7.
9. Sanderson NA, Katz M *et al*. The fate of hypertonic saline administered during hemodialysis. *Am Nephrol Nurse Assoc J* 1994; 21: 162-9.
10. Raja RM, Kramer MS, Rosenbaum JL *et al*. Use of mannitol in hemodialysis. *Dial Transplant* 1976; 5: 32-40.
11. Bergonzi G, Paties C, Vassallo G, Zangrandi A, Poisetti PG, Ballochi S, Fontana F, Scarpioni L. Dextran deposits in tissues of patients undergoing hemodialysis. *Nephrol Dial Transplant* 1990; 5: 54-8.
12. Better OS, Rubinstein I, Winaver JM, Knochel P. Mannitol therapy revisited (1940-1997). *Kidney Int* 1997; 51: 886-94.
13. Conte G, Dal Canton A, Imperatore P, De Nicola L, Gigliotti G, Pisenti A, Memoli B, Fuiano G, Esposito C, Andreucci VE. Acute increase in plasma osmolality as a cause of hyperkalemia in patients with renal failure. *Kidney Int* 1990; 38: 301-7.
14. Rodriguez M, Llach F, Pederson JA, Palma A. Changes in plasma oncotic pressure during isolated ultrafiltration. *Kidney Int* 1982; 21: 519-23.
15. Cochrane Injuries Group Albumin Reviewers. Human albumin administration in critically ill patients: systemic review of randomized controlled trials. *Br Med J* 1998; 317: 235-240.
16. The Criteria Committee of the New York Heart Association: Diseases of the Heart and Blood Vessels: Nomenclature and Criteria for Diagnosis, 6th edition, Boston, Little, *Brown & Co.,* 1964.
17. Daugirdas J. Second generation logarithmic estimates of single-pool variable volume Kt/V: an analysis error. *J Am Soc Nephrol* 1993; 4: 1205-13.
18. Feltrow CW, Baiche T, James G, Iqubal Z. Development of a treatment protocol for hemodialysis-induced hypotension. *Formulary* 1996; 31: 126-31.
19. Daugirdas JT *et al*. Dialysis hypotension: a hemodynamic analysis. *Kidney Int* 1991; 39: 233-246.
20. Bergstrom J, Asaba H, Furst P, Oules R. Dialysis, ultrafiltration, and blood pressure. *Proc Eur Dial Transplant Assoc* 1976; 13: 293-7.
21. Fox SD, Henderson LW *et al*. Cardiovascular response during hemodialysis and hemofiltration: thermal, membrane and cathecolamine influences. *Blood Purif* 1993; 11: 224-36.
22. Sherman RA *et al*. The pathophysiologic basis for hemodialysis-related hypotension. *Semin Dial* 1988; 2: 136-42.

23. Wizeman V, Leibinger A, Mueller, K, Nilson A. Influence of hydration state on plasma volume changes during ultrafiltration. *Artif Organs* 1995; 19: 416-9.
24. Mann H, Ernst E, Gladziwa U, Schallenberg U, Stiller S. Changes in blood volume during dialysis are independent upon the rate and amount of ultrafiltrate. *Trans Am Soc Artif Intern Organs* 1989; 35: 150-2.
25. Fleming SJ, Wilkinson JS, Aldrige C *et al*. Blood volume changes during isolated ultrafiltration aand combined ultrafiltration-dialysis. *Nephrol Dial Transplant* 1988; 3: 272-6.
26. Van der Sande FM, Kooman JP, Barendregt JNM, Nieman FHM, Leunissen KML. Ffect of intravenous aline, albumin, or hydroxyethylstarch on blood volume during combined ultrafiltration and hemodialysis. *J Am Soc Nephrol* 1999; 10: 1303-8.
27. Van der Sande FM, Luik AJ, Kooman JP, Verstappen V, Leunissen KLM. Effect of intravenous fluids on blood pressure course during hemodialysis in hypotensive-prone patients. *J Am Soc Nephrol* 2000; 11: 550-5.
28. Knoll GA, Grabowski JA, Dervin GF, O'Rouke K. A randomized, controlled trail of albumin versus saline for treatment of intradilytic hypotension. *J Am Sic Nephrol* 2004; 15: 487-92.
29. Gong R, Lindberg J, Abrams J, Whitaker WR, Wade CE, Gouge S. Comparison of hypertonic saline and dextran in dialysis-induced hypotension. *J Am Soc Nephrol* 1993; 3: 1808-12.
30. Nette RW, Krepel HP, van den Meiracker AH, Weimar W, Zietse R. Specific effect of the infusion of glucose on blood volume during haemodialysis. *Nephrol Dial Transplant* 2002; 17: 1275-80.
31. Kes P *et al*. Biocompatibility of dialysis membrane. *Acta Med Croatica* 1999; 53: 29-40.
32. Kes P, Bašić-Jukić N, Brunetta B *et al*. Biologic adequacy-what does it mean? *Acta Med Croat* 2004; 58: 1-4.
33. Nette RW, Ie EHY, Vletter WB, Krams R, Weimar W, Zietse R. Norepinephrine-induced vasoconstriction results in decreased blood volume in dialysis patients. *Nephrol Dial Transplant* 2006; 21: 1305-11.
34. Emili S, Black NA, Paul RV *et al*. A protocol-based treatment for intradialytic hypotension in hospitalized hemodialysis patients. *AJKD* 1999; 33: 1107-14.
35. American Thoracic Society Documents. Evidence-based colloid use in the critically ill: American thoracic society consensus statement. *Am J Respir Crit Care Med* 2004; 170: 1247-59.