Journal of Medical Sciences

ISSN 1682-4474

science alert

ANSInet
an open access publisher
http://ansinet.com

Research Paper

JMS (ISSN 1682-4474) is an International, peer-reviewed scientific journal that publishes original article in experimental & clinical medicine and related disciplines such as molecular biology, biochemistry, genetics, biophysics, bio-and medical technology. JMS is issued eight times per year on paper and in electronic format.

For further information about this article or if you need reprints, please contact:

Dr. Azza M.O. Abdel Rahman
5 Said Bahgat Street, Heliopolis,
Postal Code: 11351, Cairo, Egypt

Tel: + (202) 6366932
Fax: + (202) 4446852

ANSInet
Asian Network for Scientific Information

J. Med. Sci., 7 (2): 210-215
15th February, 2007

Relationship Between Volume Status and Blood Pressure in Children with End Stage Renal Disease on Chronic Hemodialysis

[1]Fatina I. Fadel, [1]Samar M. Sabry, [2]Azza M.O. Abdel Rahman,
[2]Emad Eldin E. Salama and [2]Marwa M. El-Sonbaty

The aim of present study was to determine the effect of interdialytic fluid accumulation (or intradialytic fluid removal) on blood pressure in pediatric patients with End Stage Renal Disease (ESRD) on chronic hemodialysis. Fifty patients with end stage renal disease on maintenance hemodialysis were enrolled in the study. They included 32 males and 18 females; age ranged from 2-16 years. We determined the association of the intradialytic decrease in blood pressure with the intradialytic decrease in plasma volume and body weight. The intradialytic decrease in plasma volume was calculated by measuring the pre- and postdialysis plasma proteins using the following equation: $\Delta PV = (PV_{pre}-PV_{post})/PV_{pre} = (TP_{post}-TP_{pre})/TP_{post}$. We found a significant positive correlation between both intradialytic decrease in systolic, diastolic and mean blood pressures and predialysis systolic, diastolic and mean blood pressures versus the decrease in plasma volume and body weight. Also, the highest decrease in plasma volume and body weight was found in the first session of the week (longest interdialytic period) compared to the 2nd and 3rd sessions of the week. Volume status influences both predialysis and postdialysis blood pressure. The effect of volume status on blood pressure may be higher in pediatric population than adults.

Key words: Volume status, blood pressure, chronic hemodialysis, pediatrics

[1]Department of Pediatrics, Faculty of Medicine, Cairo University,
[2]Department of Pediatrics, National Research Center, Dokkie, Cairo, Egypt

INTRODUCTION

Hypertension is a major cause of cardiac disease in patients on hemodialysis (Purcell *et al*., 2004). The pathogenesis of hypertension is multifactorial and is not completely understood (Kuhlmann *et al*., 2005), yet hypervolemia has always been considered a major pathogenic factor (Lopez-Gomez *et al*., 2005). Whereas control of blood pressure in hemodialysis patients using anti-hypertensive medications is feasible, recent work has emphasized that the better control of fluid status would more effectively prevent the damaging effects of fluid overload and hypertension while avoiding the side effects of anti-hypertensive medications (Steuer *et al*., 1998).

There are several studies that assessed the effect of volume status on blood pressure (Kirchner, 1997; Luik *et al*., 1997; Jain *et al*., 2001; Leypoldt *et al*., 2002; Michael *et al*., 2004) These studies, however, showed conflicting data. In addition, most of these studies were performed in adults (Kirchner, 1997; Luik *et al*., 1997; Jain *et al*., 2001); very few data on children are published (Jain *et al*., 2001; Michael *et al*., 2004). The present study aimed to assess the correlation between hypertension and excess volume parameters in pediatric patients with end stage renal disease on chronic hemodialysis, to show whether adequate control of volume status and adequate estimation of dry weight would effectively normalize blood pressure in this population. Pre- and post dialysis plasma proteins were used to calculate the intradialytic change in plasma volume. A previous study used the same approach on adult population (Leypoldt *et al*., 2002).

MATERIALS AND METHODS

The study was performed on 50 pediatric patients with ESRD undergoing maintenance hemodialysis in the Center of Pediatric Nephrology and Transplantation, Children Hospital, Cairo University. Patients who recently started hemodialysis with unidentified dry weight were excluded from the study.

Hemodialysis machines with volumetric control (Fresenius Medical Care 4008B and 4008S) were used. The standard dialysis bath consisted of sodium 135 mEq L^{-1}, potassium 2 mEq L^{-1}, calcium 3 mEq L^{-1} and bicarbonate 35 mEq L^{-1}. Dialysis prescription was based on delivering a minimum single-pool Kt v^{-1} of 1.2. Dialysis session duration ranged from 2.5-3.5 h. Blood pump flow ranged from 80-180 mL min^{-1}. Dialysis sessions were prescribed 3 times/week in most patients except for 4 patients who were dialyzing 4 times/week. The ultrafiltration rate was programmed to reach the patient's optimal dry weight which is defined as the post dialysis body weight below which the patients developed symptomatic hypotension or muscle cramps in the absence of edema (Purcell *et al*., 2004). Dialyzer size was chosen to match each patient's body surface area and to limit the circuit extracorporeal volume to <10% of patient's total body volume. Filters used were polysulfone (Fresenius USA) with surface areas 0.4, 0.7, 1.0, or 1.3 for F3, F4, F5 and F6, respectively. The dialysate flow rate (Qd) was 500 mL min^{-1}. Heparin was used for anticoagulation. Some patients had heparin free dialysis, for example those having thrombocytopenia or bleeding tendency.

We prospectively studied 150 sessions in 50 patients; the 3 sessions of the week were included for every patient. Data collected from the patients included demographic data, original renal disease, dry weight, antihypertensives given, co-morbid conditions, dialysis prescription and efficiency of dialysis as measured by Kt v^{-1} calculated in the month of the study.

Pre- and post dialysis body weights were measured by a standardized digital scale, pre- and post dialysis blood pressures were measured using a standardized mercurial sphygmomanometer with the patient in the sitting position. Predialysis blood samples were taken directly from the blood line and post dialysis samples taken from the arterial side after reducing pump speed for 30 sec. Blood samples were centrifuged after collection and the plasma was sent for determination of total protein concentration by electrochemiluminescence. The test is performed on the dimension Dade Behring.

The intradialytic decrease in body weight, mean arterial blood pressure and intradialytic change in blood pressure were calculated.

The intradialytic decrease in plasma volume was calculated from the pre- and post dialysis total protein concentrations and expressed as a percentage of the plasma volume at the beginning of hemodialysis. It was calculated using the following equation:

$$\Delta PV = (PV_{pre}\text{-}PV_{post})/PV_{pre} = (TP_{post}\text{-}TP_{pre})/TP_{post}$$

(Leypoldt *et al*., 2002)

Where TP denotes the total plasma protein concentration and subscripts pre and post denote predialysis and postdialysis values, respectively.

Statistical analysis: SPSS for Windows, version 7.5 computer program was used for statistical analysis. A p value of less than 0.05 was considered statistically significant. Data are represented as the mean±SD. The t-test was used to compare between two independent means. Paired-Samples t-test was used to compare between two dependent means. One-way analysis of variance was used to compare between more than 2 independent means. Pearson correlation coefficient r was used to measure the linear relationship between different continuous variables. Multiple regression analysis was used to provide us with an equation to estimate value of criterion (dependable) variable using values in predictor variables.

RESULTS

The study included 50 patients with ESRD on maintenance hemodialysis. Their age ranged from 2-16 years (mean age 9.98±3.32 years); their weight ranged from 7.6-45 kg (mean 21.58±7.0 kg). They consisted of 32 males and 18 females with a male to female ratio of 1.8:1.

Most of patients had an unknown etiology of renal disease (46%). The most common known etiology was obstructive uropathy (28%), followed by cystinosis (8%), focal segmental glomerulosclerosis (6%), primary oxalosis (4%), polycystic kidney disease (2%), hemolytic uremic syndrome (2%), medullary cystic disease of the kidney (2%) and mesangioproliferative glomerulonephritis (2%).

Only 8 of our patients (16%) were not receiving anti-hypertensive medications, 19 patients (38%) were receiving 1 drug, 19 patients (38%) were receiving 2 drugs and 4 patients (8%) were using 3 drugs. Nifedipine was the most commonly used anti-hypertensive (38/42, 90% of hypertensive patients) followed by captopril (25/42, 59% of hypertensive patients) and prazocin (6/42 patients, 14.2% of hypertensive patients).

A statistically significant drop of systolic, diastolic and mean blood pressures occurred following the hemodialysis sessions (Table 1).

The intradialytic decrease in body weight ranged from 0.1-2.5 kg with a mean of 0.99±0.54. The plasma protein concentration increased after dialysis; predialysis values ranged from 4.2-7.8 mg dL^{-1} (mean 6.1±0.63) and post dialysis values ranged from 5.0-11.3 mg dL^{-1} (mean 7.0±1.02).

The pre- and post dialysis plasma protein concentrations were used to calculate the percent of decrease of plasma volume. It ranged from 15-40% (mean 17±9%).

There was a significant positive correlation between intradialytic decrease in systolic, diastolic and mean blood pressures with decrease in plasma volume % (Fig. 1A-C), as well as with decrease in body weight ($r = 0.27$, $p = 0.001$, $r = 0.37$, $p<0.001$; $r = 0.23$, $p = 0.005$,

Table 1: Mean±SD systolic, diastolic and mean blood pressures before and after hemodialysis session

Variable	Systolic blood pressure (mm Hg)	Diastolic blood pressure (mm Hg)	Mean blood pressure (mm Hg)
Pre-dialysis	125.37±17.3	82.70±0.97	96.67±13.82
Post-dialysis	106.40±11.6	69.73±0.73	81.33±10.05
p-value	<0.001	<0.001	<0.001

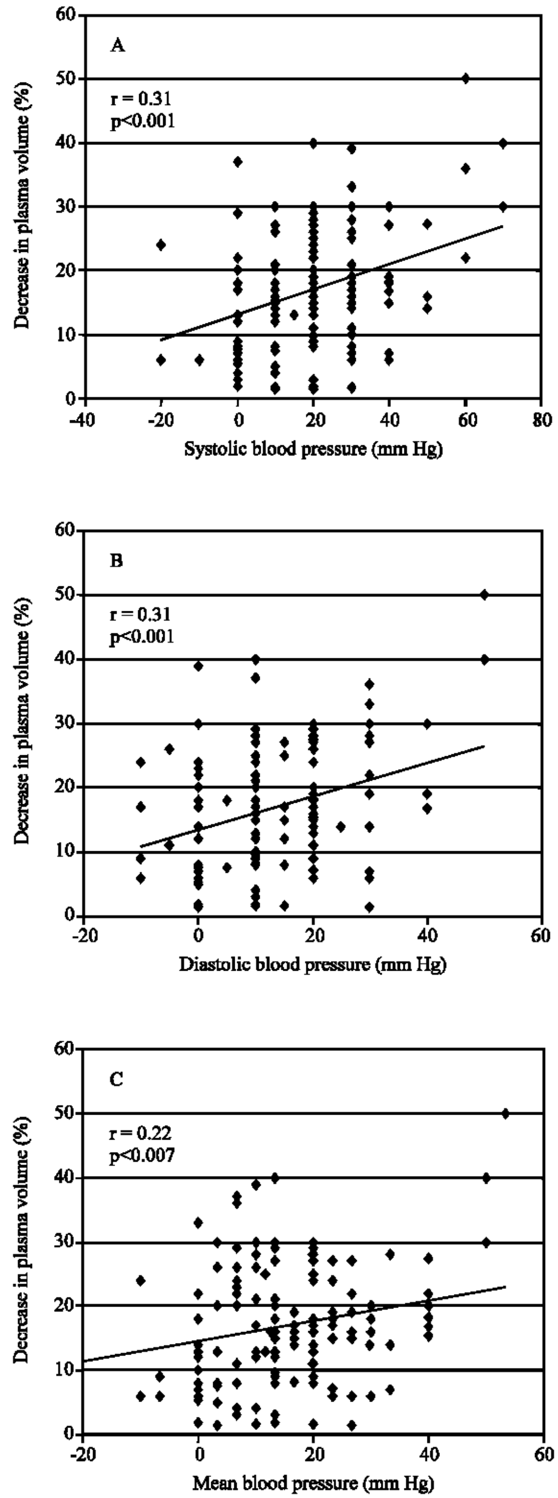

Fig. 1: Scatter diagrams and regression lines of Intradialytic decrease in systolic (A), diastolic (B) and mean blood pressure (C) versus decrease in plasma volume percent

Table 2: Correlation (r) between predialysis systolic, diastolic and mean blood pressures versus intradialytic decrease in body weight and plasma volume %

	Pre-dialysis systolic blood pressure (mm Hg)		Pre-dialysis diastolic blood pressure (mm Hg)		Pre-dialysis mean blood pressure (mm Hg)	
Variable	r	p-value	r	p-value	r	p-value
Intradialytic decrease in body weight (kg)	0.48	<0.001	0.47	<0.001	0.38	<0.001
Intradialytic decrease in plasma volume (%)	0.37	<0.001	0.38	<0.001	0.37	<0.001

Table 3: Intradialytic decrease in plasma volume % and body weight % in relation to the order of the session

Variable	Decrease in plasma volume % (mean±SD)	p-value	Decrease in body weight % (mean±SD)	p-value
Group 1 (beginning of week)	0.21±0.09*	<0.001	1.098±0.62	0.17
Group 2 (middle of week)	0.15±0.09		0.89±0.46	
Group 3 (end of week)	0.14±0.09		0.98±0.51	

*There is a statistically significant difference between Group 1 versus Groups 2 and 3 (p<0.05)

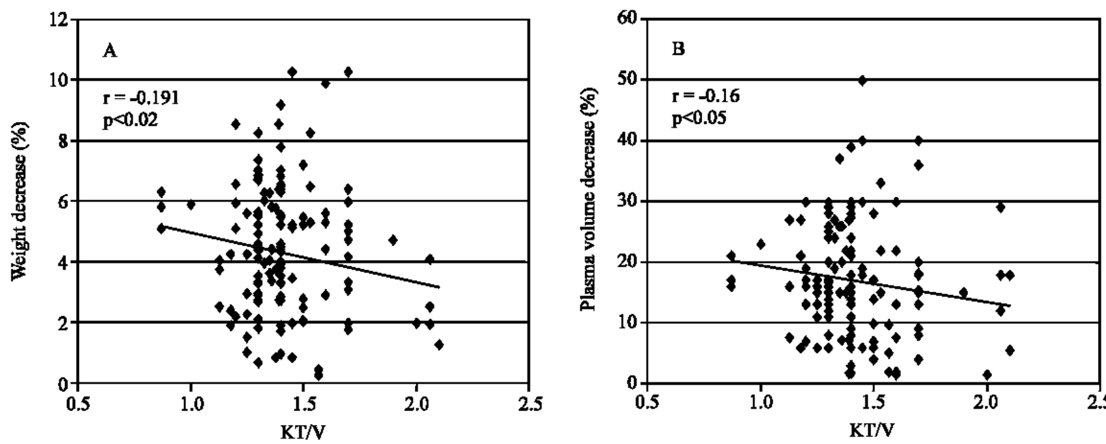

Fig. 2: Scatter diagrams and regression lines of Kt v^{-1} versus decrease in body weight percent (A) and plasma volume percent (B)

respectively). Also significant positive correlations between predialysis systolic, diastolic and mean blood pressures versus decrease in body weight and plasma volume % were present (Table 2).

We calculated the decrease of body weight as a percent of total patient's body weight instead of being used as an absolute number, in order to normalize this decrease to patient's size; and correlated this with the same parameters. Similar results were obtained.

Regression analysis showed that each 1 kg decrease of body weight was associated with 19 mm Hg decrease in systolic blood pressure and 13 mm Hg decrease in diastolic blood pressure and each 10% decrease of plasma volume was associated with 15 mm Hg decrease in systolic blood pressure and 10.5 mm Hg decrease in diastolic blood pressure.

The correlation between the KT V^{-1} (which is a measure of dialysis efficiency) with the percent of decrease in body weight and decrease of plasma volume is shown in Fig. 2A and B.

Correlation of the intradialytic decrease in plasma volume and body weight percents with the order of the session is shown in Table 3.

DISCUSSION

Hypertension is common in chronic hemodialysis patients and likely contributes to the excess morbidity and mortality in these patients (Port *et al*., 1999; Mazzuchi *et al*., 2000). Several previous studies have examined the effect of interdialytic weight gain or intradialytic reduction in body weight on blood pressure (Charra and Chazot, 2003; Kuhlmann *et al*., 2005). However, this approach does not assess postdialysis volume status. Moreover, the vast majority of these studies were performed in adults. In our study, we determined the association of the intradialytic decrease in body weight (as an indicator of interdialytic fluid gain) and the intradialytic decrease in plasma volume (as an indicator of postdialysis volume status) with predialysis and the intradialytic drop of blood pressure in pediatric patients.

The percent of hypertensive patients in our study (84%) was higher than in other studies. In a study by Grekas *et al*. (1998) which included 113 patients on regular hemodialysis, 46 patients (40%) were not receiving antihypertensives, 26% were receiving 1 drug, 22% were receiving 2 drugs and 10.5% were receiving 3 drugs. In the study by Chen *et al*. (2002) only 51% of their patients were hypertensive. Both studies were performed in adults. In the study performed in children by Sorof *et al*. (1999) the percent of hypertensive patients was also lower than in our study where only 5 of 12 patients (41.6%) were hypertensive, whereas in another study by Michael *et al*. (2004) 40% of hemodialysed children required anti-hypertensive medication. This higher percent of hypertensive patients in our study may be due to the lower age range of our patients, even when compared to studies performed in children. The low compliance to antihypertensive drugs and difficulty of dietary regulation may explain this situation.

The intradialytic decrease of plasma volume was calculated as a fraction of the predialysis value by an equation using the change in plasma protein concentration. The percent of decrease of plasma volume ranged from 1.5-40% with a mean of 17±9%. Some studies have proposed alternative methods of evaluating postdialysis volume status such as the diameter of the inferior vena cava (Katzarski *et al*., 1997), the plasma concentration of atrial natriuretic peptide (Zucchelli *et al*., 2001; Wallin *et al*., 2004), extracellular volume assessed by multifrequency bioelectric impedance (Katzarski *et al*., 1997), or total body water volume assessed by single frequency bioelectric impedance (Dionisio *et al*., 1997; Lins *et al*., 1997). In other studies which used plasma proteins for assessment of postdialysis volume status (Leypoldt *et al*., 2002; Kuhlmann *et al*., 2005) the mean decrease of plasma volume was approximately 10±9.5% which is lower than that of our study. Their studies, however, were conducted in adults. This shows that the volume overload may play a more important role in pathogenesis of hypertension in children than in adults with ESRD on maintenance hemodialysis.

In the present work, intradialytic decrease of systolic, diastolic and mean blood pressures were significantly correlated with intradialytic decrease of body weight and plasma volume percent, in contrast to Leypoldt *et al*. (2002) who found positive correlation with the decrease in systolic blood pressure only. They attributed this to the relative difficulty in accurately measuring diastolic blood pressure.

There was a significant positive correlation between the magnitude of decrease of body weight and plasma volume with predialysis systolic, diastolic and mean blood pressures ($p<0.001$ in all), which indicates that larger interdialytic weight gain leads to higher predialysis blood pressures in agreement with Grekas *et al*. (1998) and Leypoldt *et al*. (2002). However, Sherman *et al*. (1993) in their study reported only limited correlation between interdialytic weight gain and predialysis blood pressure. In a study by Fishbane *et al*. (1996) they have prolonged the dialysis time to 8 h/session to allow for complete fluid removal. They reported that <2% of their patients continued to require antihypertensive medications and concluded that volume may be the primary cause of hypertension in the vast majority of hemodialysis patients and that dialysis-refractory hypertension may simply be due to inadequate volume removal.

All analyses were performed using the magnitude of the intradialytic decrease in body weight not normalized by patient size, so we had performed similar analyses using this parameter as a percent of total body weight. We correlated the percent of decrease of body weight with the predialysis systolic and diastolic blood pressures and found a significant positive correlation. We then correlated the percent of decrease of body weight with reduction of systolic and diastolic blood pressures (the difference between the pre- and post dialysis blood pressures) and also a positive significant correlation was found. This may indicate that the use of absolute decreases of body weight and the percent of decrease of body weight give nearly identical results. This is in agreement with Leypoldt *et al*. (2002) who reached a similar conclusion.

We looked for an association between Kt v^{-1} and the volume status. We found that the more the Kt v^{-1}, the more the decrease in percent of body weight and plasma volume and this association was statistically significant. This may be explained by the fact that calculation of Kt v^{-1} uses time, ultrafiltration and postdialysis weight as parameters, in addition to pre- and post dialysis blood urea and thus prolonging time of dialysis and more ultrafiltration is expected to lead to a higher Kt v^{-1}. Whether these higher values really indicate a better dialysis efficiency needs to be further investigated. As mentioned before, when dialysis time was prolonged to increase ultrafiltration in the study by Fishbane *et al.* (1996) this led to more control of blood pressure but they did not correlate this with the Kt v^{-1}.

To further clarify the effect of volume status on blood pressure, correlation was done between intradialytic decrease in body weight and plasma volume with order of the session of the week. It is usual that the first session of the week shows a higher interdialytic weight gain due to the longer interdialytic interval (Harris and Stewart, 1994). Present results showed that the intradialytic decrease in body weight and the intradialytic decrease in plasma volume were highest in the first session of the week, compared to the second and third sessions, but was statistically significant only with the plasma volume reduction.

In conclusion, this study shows that volume status influences both predialysis and postdialysis blood pressure. The intradialytic reduction in body weight and plasma volume percent are helpful in describing volume status and predicting blood pressure in chronic hemodialysis patients. The effect of volume status on blood pressure may be higher in pediatric population than adults.

REFERENCES

Charra, B. and C. Chazot, 2003. Volume control, blood pressure and cardiovascular function. Lessons from hemodialysis treatment. Nephron. Physiol., 93: 94-101.

Chen, Y.C., H.H. Chen, J.C. Yeh and S.Y. Chen, 2002. Adjusting dry weight by extracellular volume and body composition in hemodialysis patients. Nephron., 92: 91-96.

Dionisio, P., M. Valenti and R. Bergia *et al*., 1997. Influence of the hydration state on blood pressure values in a group of patients on regular maintenance hemodialysis. Blood Purif., 15: 25-33.

Fishbane, S., E. Natke and J.K. Maesaka, 1996. Role of volume overload in dialysis-refractory hypertension. Am. J. Kid. Dis., 28: 257-261.

Grekas, D., G. Bamichas, D. Bacharaki, N. Goutzaridis, E. Kasimatis and A. Tourkantonis, 1998. Hypertension in chronic hemodialysis patients: Current view on pathophysiology and treatment. Clin. Nephrol., 53: 164-168.

Harris, D.C.H. and J.H. Stewart, 1994. Dialysis. Textbook of Renal Disease. 2nd Edn., Churchill Livingstone, pp: 363.

Jain, S.R., L. Smith, E.D. Brewer and S.L. Goldstein, 2001. Non-invasive intravascular monitoring in the pediatric hemodialysis population. Pediatr. Nephrol., 16: 15-18.

Katzarski, K.S., J. Nisell, I. Randmaa, A. Danielsson, U. Freyschuss and J. Bergstrom, 1997. A critical evaluation of ultrasound measurement of inferior vena cava diameter in assessing dry weight in normotensive and hypertensive hemodialysis patients. Am. J. Kid. Dis., 30: 459-465.

Kirchner, K., 1997. Hypertension in hemodialysis patients: More question than answers. Am. J. Kid. Dis., 30: 577-578.

Kuhlmann, M.K., F. Zhu, E. Seibert and N.W. Levin, 2005. Bioimpedance, dry weight and blood pressure control: New methods and consequences. Curr. Opin. Nephrol. Hypertens, 14: 543-549.

Leypoldt, J.K., A.K. Cheung, J.A. Delmez, J.J. Gassman, N.W. Levin, J.A.B. Lewis, J.L. Lewis and M.V. Rocco, 2002. Relationship between volume status and blood pressure during chronic hemodialysis. Kid. Intl., 61: 266-275.

Lins, R.L., M. Elsevters and P. Rogiers *et al*., 1997. Importance of volume factors in dialysis related hypertension. Clin. Nephrol., 48: 29-33.

Lopez-Gomez, J.M., M. Villaverde, R. Jofre, P. Rodriguez-Benitez and R. Perez-Garcia, 2005. Interdialytic weight gain as a marker of blood pressure, nutrition and survival in hemodialysis patients. Kid. Intl. Suppl., 93: S63-68.

Luik, A.J., W.H.M. van Kuik, J. Spek, F. de Heer, L.M. van Bortel, P.M.H. Schiffers, J.P. van Hoof and K.M.L. Leunissen, 1997. Effects of hypervolemia on interdialytic hemodynamics and blood pressure control in hemodialysis patients. Am. J. Kid. Dis., 30: 466-474.

Mazzuchi, N., E. Carbonell and J. Fernandez-Cean, 2000. Importance of blood pressure control in hemodialysis patient survival. Kid. Intl., 58: 2147-2154.

Michael, M., E.D. Brewer and S.L. Goldstein, 2004. Blood volume monitoring to achieve target weight in pediatric hemodialysis patients. Pediatr. Nephrol., 19: 432-437.

Port, F.K., T.E. Hulbert-Shearon and R.A. Wolfe *et al*., 1999. Predialysis blood pressure and mortality risk in a national sample of maintenance hemodialysis patients. Am. J. Kid. Dis., 33: 507-517.

Purcell, W., E. Manias, A. Williams and R. Walker, 2004. Accurate dry weight assessment: Reducing the incidence of hypertension and cardiac disease in patients on hemodialysis. Nephrol. Nurs. J. Nov-Dec; 31: 631-636.

Sherman, R.A., A. Daniel and R.P. Cody, 1993. The effect of interdialytic weight gain on predialysis blood pressure. Artig. Organs., 17: 770-774.

Sorof, J.M., E.D. Brewer and R.J. Portman, 1999. Ambulatory blood pressure monitoring and interdialytic weight gain in children receiving chronic hemodialysis. Am. J. Kid. Dis., 33: 667-674.

Steuer, R.R., M.J. Germain, J.K. Leypoldt and A.K. Cheung, 1998. Enhanced fluid removal by blood volume monitoring during chronic hemodialysis. Artif. Org., 22: 627-632.

Wallin, C.J., P. Rossi, S.H. Jacobson and L.G. Leksell, 2004. Central blood volume, atrial natriuretic peptide and intermittent hemodialysis. Scand J. Urol. Nephrol., 38: 78-84.

Zucchelli, P. and A. Santoro, 2001. Dry weight in hemodialysis: Volemic control. Semin Nephrol., 21: 286-290.