

Pharmacological and non-pharmacological treatment of hypertension in dialysis patients

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Hypertension is very common in dialysis patients. The most important cause of hypertension is hypervolemia. Fluid restriction and volume management with standard hemodialysis are effective strategies to achieve dry weight and blood pressure control without use of antihypertensive drugs. If the captopril test is positive, a renin-angiotensin system blocker should be started. The pre-dialysis blood pressure goal in hemodialysis patients should be < 140/90 mm Hg initially and < 130/80 mm Hg at 3–6 months of dialysis.

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Hypertension is an important issue to be addressed in dialysis patients. The prevalence of hypertension is still very high both in Turkey and all around the world. The most frequent etiology of hypertension in dialysis patients is impaired renal function, as the kidneys are unable to excrete water and sodium and consequently hypervolemia occurs. Although the role of hypervolemia in the etiology of hypertension is well known, this condition is difficult to treat.

The first step in management of hypertension in dialysis patients should be to achieve the dry weight, which then has to be updated and maintained accurately. In order to reach this target weight, patient compliance with dialysis treatment and volume restriction requirements is essential. Both the physician and nurse have to be aware of the importance of dry weight and must be willing to provide support to the patient to achieve this goal. A dietitian who is knowledgeable of human physiology and who appreciates the importance of salt restriction is another essential member of the dialysis unit health-care team.

To state that a dialysis patient has achieved his or her dry weight means that the patient's extracellular fluid volume must be normal. What is the exact definition of dry weight clinically? We can define dry weight simply as absence of edema, jugular vein distension, or ascites on physical examination before dialysis session, normal pre-dialysis blood pressure, and normal blood pressure after the dialysis session.

If all these criteria are met, we can then assume that the weight of a patient at the end of dialysis session is the dry weight, unless the treatment is interrupted or terminated early because of clinically significant hypotensive episodes.

First, the patient should be educated on salt restriction. Even a salt restricted diet limits daily sodium intake to 50–60 mmol (3–3.5 g salt), which will lead to 300–400 ml weight gain daily. The patient has to be advised that his weight will increase by 100–120 ml for each gram of sodium chloride consumed between dialysis sessions. Another fact that has to be appreciated is that higher salt consumption contributes to thirst and higher water intake as a result of osmoregulation. Dialysis patients have to be educated that daily consumption of 9 g of salt will lead to mandatory one liter of water intake, which will result in a significant increase in intravascular fluid, which is almost always followed by hypertension. The cardiovascular consequences

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of longstanding, poorly controlled hypertension include structural abnormalities of the heart such as hypertrophy and dilatation.¹ In addition to salt restriction, the dialysis regimen may need to be altered to help an individual patient achieve dry weight by increasing the number and duration of weekly treatments with supplemental ultrafiltration sessions if needed.^{2,3}

In general, patients receiving anti-hypertensive medications, and new hemodialysis patients lose weight and become euvolemic initially. As patients become accustomed to dialysis treatments, anabolic processes increase and weight gain may occur in the form of muscle and fat.^{2,3} Conversely, when dialysis patients are affected by an infectious process, it may be necessary to decrease dry weight targets given the increased risk of hypotension associated with systemic vasodilatation. Nephrologist has to be alert that dry weight is a dynamic measure and can change in some circumstances.

How should dry weight be monitored? This is an important question with a complex answer. The simplest solution involves trending patients' weights and evaluating for signs of hypervolemia on physical examination. Cardiothoracic index (CTI) can be calculated from a chest X-ray. Body weight measurement, interdialytic weight gain measurement, and CTI calculations are sufficient for the volume assessment of most hemodialysis patients.^{3,4} However, for hypertensive patients in whom dry weight has not been determined, use of additional methods may be required, such as echocardiography to determine left atrial diameter and vena cava index and bioimpedance to evaluate body compartments. The important thing is to follow-up and to make changes when necessary.

The importance of the captopril test to detect hypervolemia in hypertensive dialysis patients must be mentioned. If blood pressure remained $>140/90$ mm Hg, but if there is doubt whether euvoemia was reached because CTI was close to normal (<0.50), the captopril test can be used to evaluate the 'renin-dependency' of the blood pressure. This test is performed on a non-dialysis day. Blood pressure is taken at

10-min intervals with an automatic machine in a quiet room for 1 h before and at least 90 min after oral administration a tablet of 25 mg captopril. The test is considered positive when blood pressure drops to normal levels or if diastolic blood pressure drops by >10 mm Hg. If the test is positive, then a renin-angiotensin system blocker such as enalapril should be started. However, if the test is negative, measures to reduce the dry weight must be performed.⁴

Another volume measurement called refill velocity also needs to be mentioned. It is defined as the velocity of water filling back to intravascular space from the interstitial space. Under normal conditions the rate of refill is 1–1.2 l/h in humans. In hemodialysis patients, baseline conditions are never optimal because of commonly associated cardiac disorders such as dilatation, hypertrophy, or failure and hypoalbuminemia. Thus, refill velocity is not normal in these patients and changes must be assessed on an individual basis. Problems arise for dialysis patients when the rate of ultrafiltration exceeds the refill velocity, as the intravascular volume will decrease and cause hypotension. These hypotensive episodes will hinder achievement of dry weight. Therefore, the hemodialysis prescription should be individualized for each patient.⁵

Considering these physiological facts, the first approach to management of hypertension in dialysis patients can be termed 'strict volume control strategy'. This requires a two-step plan. The first one is salt restriction and the second is the determination and maintenance of the dry weight (followed by CTI). We have previously reported that normal blood pressure can be obtained with standard 4-h hemodialysis sessions thrice weekly.^{3,4,6} The most important parameter was the CTI, as the mortality risk was four times higher in the patients with a CTI >0.48 . Another important finding in this study was that the daily weight gain decreased to 0.95 kg from 1.45 kg following the implementation of measures to achieve strict volume control.⁴ Although, in this study echocardiography was not performed systematically, results were available in approximately 50% of patients in whom blood

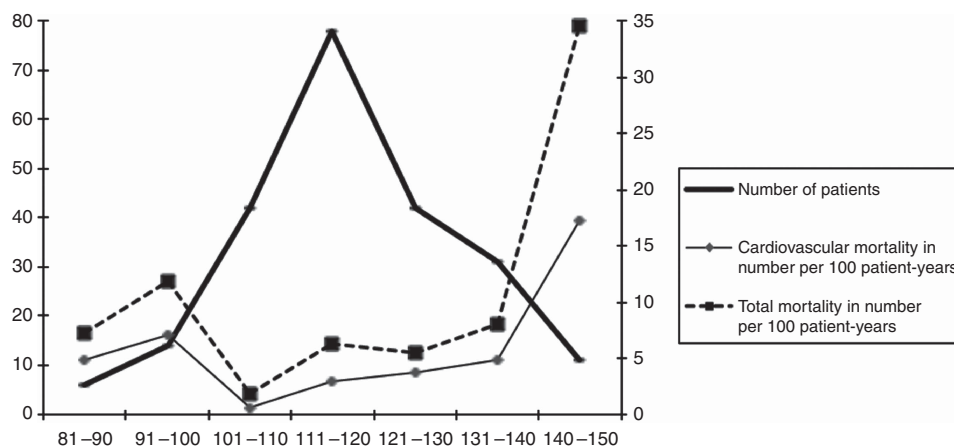


Figure 1 | Relationship between final systolic blood pressure (SBP) and mortality in number per 100 patient-years.³ The left vertical axis indicates the number of patients and right vertical axis the mortality per 100 patient-years.

pressure was well controlled. We observed that left ventricular hypertrophy was present in 66% of patients who died, while it was present in 23% of surviving patients. The CTI was significantly correlated with left ventricular mass, left ventricular end diameter, and left atrium diameter. When the available echocardiographic data were separated into groups according to the systolic blood pressure levels, there was a clear tendency for the left ventricular mass and CTI to increase in those with higher blood pressure levels.⁴ Another important finding in this study was the measures to achieve blood pressure control and the association of lower blood pressure levels with higher survival rates. Only 4% patients were on anti-hypertensive medication. All these patients had CTI > 0.48 and were on renin-angiotensin system blocker medications. Similarly, in a report from Tassin, France, < 5% of the patients treated by long hemodialysis method (8-h thrice weekly) and volume control, required anti-hypertensive drugs.² In addition, antihypertensive agents may increase the risk of severe hypotensive episodes in hemodialysis session while they are often ineffective in controlling blood pressure. If dry weight can be determined accurately, fewer than 10% of hemodialysis patients will require antihypertensive medication. In Figure 1, the systolic blood pressure distribution and mortality rate are demonstrated. It is obvious that the mortality increases as the systolic pressure exceeds 130 mm Hg although the number of patients is small. The best survival is obtained in the patient group with a systolic pressure between 100 and 130 mm Hg.⁴

Moreover, we have shown in a previously published study that the elevated CTI and left ventricular hypertrophy reversed with decreased blood pressure by strict volume control in standard hemodialysis patients.⁶ It is well known

that left ventricular hypertrophy is a significant predictor of cardiovascular mortality.⁴

In conclusion, hypertension is very common in hemodialysis patients. Extracellular fluid volume is an important determinant of blood pressure but is difficult to evaluate. Patients' awareness of salt restriction is critical. Strict volume control strategy has been shown to be an effective means to attain dry weight goals and blood pressure control without use of antihypertensive drugs on standard hemodialysis. Achievement of volume control (or dry weight target goals) will be easier if the total weekly amount of hemodialysis sessions exceeds 12 h. The pre-dialysis blood pressure goal in hemodialysis patients should be < 140/90 mm Hg at initially period and then < 130/80 mm Hg at 3–6 months of dialysis.

DISCLOSURE

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REFERENCES

1. Parfrey PS, Foley RN, Harnett JD *et al.* Outcome and risk factors for left ventricular disorders in chronic uraemia. *Nephrol Dial Transplant* 1996; **11**: 1277–1285.
2. Laurent G, Charra B. The results of an 8 h thrice weekly haemodialysis schedule. *Nephrol Dial Transplant* 1998; **13**(Suppl 6): 125–131.
3. Ozkahya M, Toz H, Unsal A *et al.* Treatment of hypertension in dialysis patients by ultrafiltration: role of cardiac dilatation and time factor. *Am J Kidney Dis* 1999; **34**: 218–221.
4. Ozkahya M, Ok E, Toz H *et al.* Long-term survival rates in haemodialysis patients treated with strict volume control. *Nephrol Dial Transplant* 2006; **21**: 3506–3513.
5. Toz H, Ozkahya M, Ozerkan F *et al.* Improvement in 'uremic' cardiomyopathy by persistent ultrafiltration. *Hemodial Int* 2007; **11**: 46–50.
6. Ozkahya M, Toz H, Ozerkan F *et al.* Impact of volume control on left ventricular hypertrophy in dialysis patients. *J Nephrol* 2002; **15**: 655–660.