

Improvement of Resistant Hypertension by Nocturnal Hemodialysis in a Patient with End-Stage Kidney Disease

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Key Words

Resistant hypertension · End-stage kidney disease · Nocturnal hemodialysis

Abstract

Resistant hypertension is a common and refractory complication of hemodialysis (HD) patients and is associated with a higher risk of cardiovascular morbidity and mortality. Here we present a case of resistant hypertension treated successfully by nocturnal HD. A 63-year-old female with end-stage kidney disease was hospitalized for severe headache, objective vertigo and persistent vomiting for 1 month on February 6, 2012. She had been on intermittent HD for 3 months, and her blood pressure maintained 200–240/100–130 mm Hg even after using 7 kinds of antihypertensive drugs including olmesartan, benazepril, nitrendipine, arotinolol, terazosin, clonidine and torasemide. A CT of the abdomen revealed a mild hyperplasia of the left adrenal gland (fig. 1). However, plasma renin, angiotensin and aldosterone were all within the normal range. Nocturnal extended HD was initiated with a blood flow rate of 150 ml/min and a dialysis time of 7 h. After 3 months of nocturnal HD, all symptoms were relieved and her systolic blood pressure started to decrease by 10–20 mm Hg. Six months later, the pre-dialysis blood pressure was decreased to 140–160/90–100 mm Hg and the antihypertensive drugs were reduced to 4 kinds. Meanwhile, the blood biochemical parameters including hemoglobin, serum calcium, phosphate and parathyroid hormone were all controlled well during 2 years of treatment. This case indicates that nocturnal extended HD is probably a promising and effective choice for resistant hypertension in HD patients.

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Introduction

Resistant hypertension is a common and refractory complication of hemodialysis (HD) patients and is associated with a higher risk of cardiovascular morbidity and mortality. In addition to the intensive antihypertensive therapies, there are many other strategies to control resistant hypertension in HD patients, such as the adjustment of their dialysis plan, sympathetic denervation and bilateral nephrectomy, etc. We herein report a case in which resistant hypertension was successfully controlled by nocturnal extended hemodialysis (NHD).

Case Report

A 63-year-old female was admitted to our hospital on February 6, 2012, due to uncontrolled hypertension despite antihypertensive treatment. She had been treated with chronic HD (F15 dialyzer, 1.5 m², polysulfone, Shandong Weigao, PR China) for end-stage kidney disease secondary to diabetic nephropathy 3 times a week for 3 months. The blood flow rate and dialysis time of each HD session was 200–220 ml/min and 4 h. The ultrafiltration volume was 1.0–1.5 liters for each session. Her postdialysis body weight was kept at 58–59 kg. She had had hypertension for 15 years and had been treated with telmisartan 80 mg b.i.d., lacidipine 4 mg b.i.d. and clonidine 150 µg t.i.d. Her blood pressure was controlled around 150/90 mm Hg. Erythropoietin (10,000 U q.w.) was used to treat anemia. Two months previously, the patient experienced headache and dizziness with a blood pressure of 235/120 mm Hg. Her postdialysis body weight was then adjusted to 55 kg in the next 2 weeks. However, there was no improvement of the blood pressure and she started to feel thirsty during the HD session. Meanwhile, the antihypertensive drugs were gradually increased to olmesartan (20 mg b.i.d.), benazepril (20 mg b.i.d.), nitrendipine (20 mg t.i.d.), arotinolol (10 mg b.i.d.), terazosin (2 mg b.i.d.), torsemide (40 mg q.d.) and clonidine (150 µg t.i.d.). Her symptoms were not relieved, and the systolic blood pressure maintained at about 180–200 mm Hg. Two days before her hospital admission, she presented with severe headache, objective vertigo, nausea and persistent vomiting, with a blood pressure in the 240/120 mm Hg. Her urine volume was about 400 ml/day on admission. The physical examinations at hospitalization showed that her blood pressure was 240/120 mm Hg without any postural change, and her pulse rate was 83/min with a regular rhythm. No abnormal finding was seen in her chest and abdomen. She had an arteriovenous shunt in the right forearm. There was no leg edema. Neurological findings showed that the bilateral Babinski sign was positive.

A blood analysis showed a white blood cell count of $8.6 \times 10^9/l$, hemoglobin of 106 g/l and a platelet count of $242 \times 10^9/l$. Her blood chemistry revealed a urea level of 13.6 mmol/l, creatinine 312 µmol/l, potassium 3.8 mmol/l, sodium 136 mmol/l, chloride ion 101 mmol/l, calcium 1.84 mmol/l and phosphate 1.65 mmol/l. The liver function was unremarkable. A CT of the head showed several lacunar infarctions and did not exhibit hemorrhage or masses. An ambulatory blood pressure measurement showed the average diurnal and nocturnal blood pressure to be 173/69 and 183/71 mm Hg, respectively, while the maximum and minimum blood pressure was 216/85 and 155/100 mm Hg. A color duplex ultrasonography of the renal artery did not suggest the presence of stenosis. A CT of the abdomen revealed mild hyperplasia of the left adrenal gland (fig. 1). However, no abnormal results were found in the endocrinological analysis. The plasma renin activity was 0.37 ng/ml (normal range 0.05–0.79 ng/ml) and a plasma aldosterone concentration of 103.85 pg/ml (normal range 59.5–173.9 pg/ml). Her serum angiotensin I and II were 0.2 and 55.65 pg/ml (normal range 28.2–

52.2 pg/ml), respectively. The serum cortisol was 318.1 µg/l (normal range 42–384 µg/l), and her plasma adrenocorticotrophic hormone level was 13.9 pg/ml (normal range 10–80 pg/ml). She was treated intravenously with urapidil hydrochloride, and the blood pressure maintained at 160–240/70–130 mm Hg.

Two weeks after admission (February 24), NHD with a Rexeed 15UC dialyzer (1.5 m², polysulfone membrane; Asahi Kasei, Japan) was initiated, with a blood flow rate of 150 ml/min and a dialysis time of 7 h on a t.i.w. regimen. Her postdialysis body weight stayed at roughly 54 kg. Erythropoietin was temporally held because of the extremely high blood pressure. After 3 months of NHD, all symptoms were remittent and her systolic blood pressure started to decrease by 10–20 mm Hg (fig. 2). Erythropoietin was then used again, and the dosage was gradually increased to 10,000 U per week. Six months later, the pre-dialysis blood pressure was decreased to 140–160/90–100 mm Hg and the antihypertensive drugs were reduced to 4 kinds (olmesartan 20 mg b.i.d., nitrendipine 20 mg t.i.d., arotinolol 10 mg b.i.d. and clonidine 150 µg t.i.d.). The patient has been on NHD for over 2 years. The most recent blood biochemical parameters including hemoglobin, serum calcium and phosphate and parathyroid hormone were 100 g/l, 2.42 mmol/l, 1.8 mmol/l and 156.5 pg/ml, respectively.

Discussion

Resistant hypertension is defined as uncontrolled blood pressure in a patient who adheres to at least 3 different antihypertensive agents at maximally tolerated doses including a diuretic [1]. Many studies have verified that chronic kidney disease (CKD) is associated with a higher risk of having resistant hypertension [2, 3]. Hypertensive patients with CKD were found to be 2.9 times more likely to have resistant hypertension than those lacking CKD [2]. Tanner et al. [3] reported that the prevalence of resistant hypertension was as high as 33% among predialysis CKD patients with a glomerular filtration rate of <45 ml/min/1.73 m². Although there is no epidemiology data about the resistant hypertension in dialysis patients, it is clear that the prevalence of hypertension in those patients is extremely high (up to 90%), and very few have satisfactory blood pressure control [4]. Hypertension is a major independent risk factor for cardiovascular disease and mortality, and patients with resistant hypertension represent a more severe subset with a fourfold risk of cardiovascular events than patients with controlled hypertension [5]. Therefore, it is very important to take various measures to control the blood pressure in CKD patients. The pathogenesis of resistant hypertension in CKD is uncertain but likely multifactorial, including the increased activity of the renin-angiotensin-aldosterone system and the renal sympathetic nervous system, a nitric oxide deficiency, oxidative stress, renal artery stenosis, hyperaldosteronism, obstructive sleep apnea and vasodilator medications [6].

In our patient, although the CT of her abdomen revealed a mild adrenal hyperplasia, the renal endocrinological analysis was unremarkable. No stenosis was observed in the renal artery by color duplex ultrasound. Unfortunately, the patient refused to perform further examinations (e.g. CTA and DSA) to rule out renal artery stenosis. Nevertheless, no conclusive evidence has been found as of yet, which proves the existence of endocrine adenopathy or renovascular hypertension. The combined use of 7 kinds of antihypertensive medications was still not efficient enough to control the blood pressure. Thus, additional options should be considered to lower blood pressure. The effective control of resistant hypertension after a period of NHD partly ruled out the possibility of endocrine adenopathy or renovascular hypertension.

Conventional HD does not normalize all abnormalities in HD patients and provides only a small fraction of small molecular weight solute clearance. In an attempt to improve the urea clearance and clinical outcomes, NHD has been developed in the last decade. Although there is no clear consensus on the impact of NHD on cardiovascular outcomes and the quality of life [7–9], almost all observational studies and controlled trials have suggested that NHD can facilitate better control of hypertension and reduce the use of antihypertensive medications [8–11]. A meta-analysis reported that both systolic and diastolic blood pressures were reduced significantly after switching to NHD [systolic blood pressure -14.1 mm Hg (95% CI -17.2 to -11.0), diastolic blood pressure -7.1 mm Hg (95% CI, -9.2 to -4.9)]. The mean number of anti-hypertensive medications was also decreased. Moreover, antihypertensive medications were withdrawn in 53.5% of patients [12]. The Frequent Hemodialysis Network (FHN) trial confirmed that NHD reduced blood pressure with fewer antihypertensive medications after 12 months [7].

One could speculate that frequent or extended HD might provide better control of the extracellular fluid volume as well as the removal of neurohumoral variables involved in hypertension and cardiac remodeling, which, in turn, may lead to the beneficial change of blood pressure. Nevertheless, a systemic analysis performed in 2005 did not find a significant difference of extracellular fluid volume between conventional and nocturnal groups, despite a remarkable reduction in blood pressure or in the number of antihypertensive medications [10], which indicated that there are probably other mechanisms involved. There was no distinct body weight change in our patient either. Some studies pointed out that decreased arterial resistance and improved endothelial function might have contributed [11]. Chan et al. [11] used a noninvasive method to measure the arterial compliance in NHD patients who converted from conventional HD. After 2 months of treatment, there was a substantial fall in the total peripheral resistance as well as the systemic arterial pressure. The heart rate modulation was significantly increased by the arterial baroreflex. In another study, the author reported that NHD restored endothelium-dependent and endothelium-independent vasodilation of a muscular artery as well [13]. In contrast, no effect was observed on arterial baroreflex sensitivity in conventional HD patients [14]. Thus, the author suggested that NHD might decrease the systemic and peripheral artery resistance by promoting structural or functional vascular changes.

Besides the improvements in blood pressure control, the blood biochemical parameters of our patient including hemoglobin, serum calcium and phosphate and parathyroid hormone were all well-controlled during 2 years of treatment. This was consistent with the findings in previous case-control studies. Culeton et al. [15] reported that NHD was associated with a better control of the mineral metabolism, including a reduction in or discontinuation of oral phosphate binders. Certainly, the additional dialysis time spent undergoing NHD probably played an important role in improved solute control as well.

Conclusion

Resistant hypertension is commonly seen in CKD patients. NHD might improve the blood pressure by removing excess extracellular fluid volume and neurohumoral factors as well as decreasing the systemic and peripheral artery resistance. This case indicates that NHD is probably a promising and effective choice for the resistant hypertension in hemodialysis patients.

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Disclosure Statement

The authors declare that they have no competing interests.

References

- 1 National High Blood Pressure Education Program: The seventh report of the Joint National Committee on prevention, detection, evaluation, and treatment of high blood pressure. *Hypertension* 2003;42:1206–1252.
- 2 Chia YC, Ching SM: Prevalence and predictors of resistant hypertension in a primary care setting: a cross-sectional study. *BMC Fam Pract* 2014;15:131.
- 3 Tanner RM, Calhoun DA, Bell EK, et al: Prevalence of apparent treatment-resistant hypertension among individuals with CKD. *Clin J Am Soc Nephrol* 2013;8:1583–1590.
- 4 Agarwal R, Nissenson AR, Batlle D, Coyne DW, Trout JR, Warnock DG: Prevalence, treatment, and control of hypertension in chronic hemodialysis patients in the United States. *Am J Med* 2003;115:291–297.
- 5 Pierdomenico SD, Lapenna D, Bucci A, et al: Cardiovascular outcome in treated hypertensive patients with responder, masked, false resistant, and true resistant hypertension. *Am J Hypertens* 2005;18:1422–1428.
- 6 Khawaja Z, Wilcox CS: Role of the kidneys in resistant hypertension. *Int J Hypertens* 2011;2011:143471.
- 7 Chan CT, Greene T, Chertow GM, et al: Determinants of left ventricular mass in patients on hemodialysis: Frequent Hemodialysis Network (FHN) Trials. *Circ Cardiovasc Imaging* 2012;5:251–261.
- 8 Rocco MV, Lockridge RS Jr, Beck GJ, et al: The effects of frequent nocturnal home hemodialysis: the Frequent Hemodialysis Network Nocturnal Trial. *Kidney Int* 2011;80:1080–1091.
- 9 Manns BJ, Walsh MW, Culleton BF, et al: Nocturnal hemodialysis does not improve overall measures of quality of life compared to conventional hemodialysis. *Kidney Int* 2009;75:542–549.
- 10 Walsh M, Culleton B, Tonelli M, Manns B: A systematic review of the effect of nocturnal hemodialysis on blood pressure, left ventricular hypertrophy, anemia, mineral metabolism, and health-related quality of life. *Kidney Int* 2005;67:1500–1508.
- 11 Chan CT, Jain V, Picton P, et al: Nocturnal hemodialysis increases arterial baroreflex sensitivity and compliance and normalizes blood pressure of hypertensive patients with end-stage renal disease. *Kidney Int* 2005;68:338–344.
- 12 Susantitaphong P, Koulouridis I, Balk EM, et al: Effect of frequent or extended hemodialysis on cardiovascular parameters: a meta-analysis. *Am J Kidney Dis* 2012;59:689–699.
- 13 Chan CT, Harvey PJ, Picton P, et al: Short-term blood pressure, noradrenergic, and vascular effects of nocturnal home hemodialysis. *Hypertension* 2003;42:925–931.
- 14 Agarwal A, Anand IS, Sakhuja V, Chugh KS: Effect of dialysis and renal transplantation on autonomic dysfunction in chronic renal failure. *Kidney Int* 1991;40:489–495.
- 15 Culleton BF, Walsh M, Klarenbach SW, et al: Effect of frequent nocturnal hemodialysis vs conventional hemodialysis on left ventricular mass and quality of life: a randomized controlled trial. *JAMA* 2007;298:1291–1299.

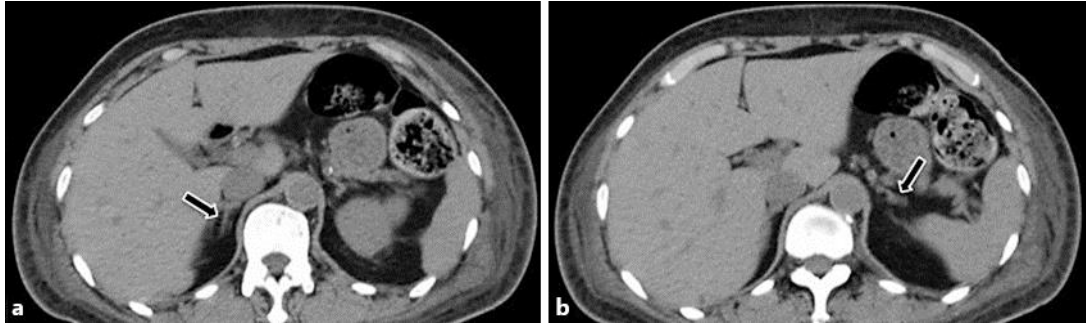


Fig. 1. CT images of the adrenal glands. No abnormality was observed (**a**, arrow), however, there was a slight enlargement in the lateral branch of the left adrenal gland (**b**, arrow). Plasma renin, angiotensin and aldosterone were all within normal range.

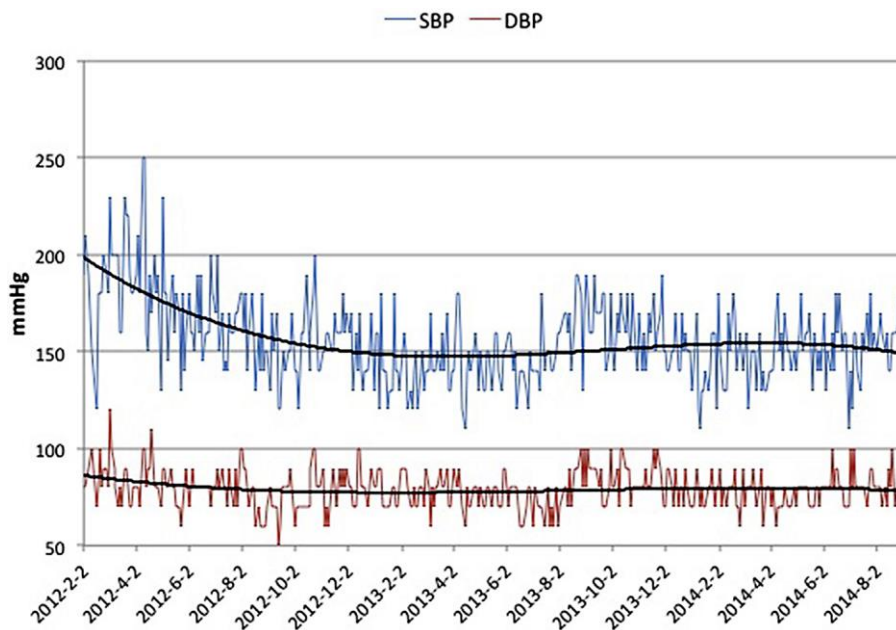


Fig. 2. The predialysis blood pressure of the patient during a 2-year cycle of NHD. The patient started NHD on February 24, and her systolic blood pressure (SBP, blue line) started to decrease by 10–20 mm Hg after 3 months. Six months later, the predialysis systolic blood pressure decreased to 140–160/90–100 mm Hg and remained stable thereafter. DBP = Diastolic blood pressure.