

Renal denervation in patients with resistant hypertension-beyond blood pressure reduction

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ABSTRACT

Renal sympathetic denervation (RDN) has been demonstrated as an antihypertensive treatment in resistant hypertension patients, and triggers additional positive effects on glucose metabolism and insulin sensitivity in type 2 diabetes. The clinical implications of RDN in patients with type 2 diabetes, diabetic nephropathy and resistant hypertension have not yet been fully defined.

We hypothesized that the small antihypertensive effects of RDN treatment will induce additional benefits on renal function in CKD patients with type 2 diabetes and resistant hypertension.

We report the effects of RDN in two patients with type 2 diabetes, diabetic nephropathy, stage 3 chronic kidney disease and resistant hypertension. The blood pressure (BP) reduction after RDN was an 8-9% reduction of ABPM (sustained at consecutive follow-up visits at 3 and 6 months when compared to the baseline) and restoration of the night time dipping pattern was associated with amelioration of albuminuria (UAR).

As proteinuria may accelerate kidney disease progression to end-stage renal failure, recognition of the antiproteinuric treatment is essential for providing renoprotection. Therefore, randomized clinical trials are required to assess the impact of reported changes.

Key words: resistant hypertension, renal denervation

Introduction

Diabetes and hypertension are two main causes of chronic kidney disease (CKD) and diabetic nephropathy is the leading cause of end-stage renal disease (ESRD). (1,2) Chronic kidney disease is responsible for sympathetic nervous system hyperactivation that leads to fluid overload, aggravation of hypertension and further deterioration and loss of renal function. (3) Despite the available pharmacological inhibition of the sympathetic nervous system, pharmacotherapy does not provide adequate effects in clinical practice; thus, renal sympathetic denervation (RDN) which produces multilevel inhibi-

tion of the sympathetic nervous system, that triggers additional positive effects on glucose metabolism and insulin sensitivity, could be a therapeutic option for treating resistant hypertension in CKD patients. (4-7)

Case reports

We present male patients (66 and 57-years-old respectively) with resistant hypertension (RH), diabetes (type 2: HbA1c 6.6 and 7.1%) with diabetic nephropathy (increased urinary albumin excretion (UAE) with no hematuria and normal kidney ultrasound dimensions) and chronic kidney disease grade III (eGFR-MDRD 30 and 34 ml/min/1.73m²). Before the RDN intervention, antihypertensive treatment was optimized (BHS/NICE treatment

algorithm), and non-concordance with pharmacotherapy and secondary forms of hypertension were excluded. Blood pressure was resistant to treatment with six antihypertensive drugs from different classes (diuretic, angiotensin-converting enzyme inhibitor or angiotensin receptor blocker, calcium channel blocker, direct vasodilator (urapidil), centrally acting sympatholytic (moxonidine) and aldosterone antagonist (spironolactone)), statin therapy and oral hypoglycemic drugs. The RDN method, and its risks and benefits were explained to the patients and written consent was obtained. After the RDN procedure, the patients were stable and without a worsening of renal function. The 24-hour ambulatory blood pressure monitoring (ABPM)

and laboratory analysis were assessed at baseline (before RSD) and at 3 and 6 month follow-up visits. The ABPM revealed hypertension with non-dipping BP pattern before RDN. The blood pressure (BP) reduction after RDN was an 8-9% reduction of ABPM (sustained at follow-up visits at 3 and 6 months when compared to the baseline). The RDN restored the dipping BP pattern. An additional positive effect was observed on proteinuria alleviation: after the procedure UAE was 7.9 mg/mmol in the first patient (before RDN 8.3), and 30 mg/mmol in the second patient (before RDN 400) with a stable value of HbA1c (6.5 and 6.9%).

Discussion

Resistant hypertension is associated with a hyperactive sympathetic nervous system and directly linked with a high risk of target organ damage. (5,6,7) Normal circadian BP rhythm includes nocturnal BP decline – the dipping BP pattern (more than 10% sleep-time relative BP decline). In patients with type 2 diabetes, a non-dipping pattern is highly correlated with the rate of UAE; 80% of patients with albuminuria A3 (UAE >30 mg/mmol/L) were found to have loss of sleep-time BP decline. (8) The non-dipping BP pattern is associated with a lesser BP response to antihypertensive medication, accelerates kidney disease

progression to end-stage renal failure and increases the risk of cardiovascular complications. (8) Evidence of RDN reducing office BP levels and restoring dipping pattern in a small series of 15 patients with mean eGFR 31 mL/min/1.73m² were reported; but with no significant decrease in proteinuria. (7)

Conclusion

Due to potentially beneficial multiple risk factor reductions, as well as safety concerns, a focused assessment of already obtained data from patients with type 2 diabetes, diabetic nephropathy and resistant hypertension after RDN intervention should be of importance.

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