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RESISTANT HYPERTENSION – RAY OF HOPE

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Hypertension has assumed the status of a major health problem effecting 40% population above the age of 60 years. The causal relationship with stroke, left ventricular hypertrophy, heart failure and renal failure has been established beyond any doubt. Adequate hypertension control remains a challenge even in the advanced countries. Resistant hypertension, defined as failure to achieve target blood pressure despite concurrent use of 3 antihypertensive agents of different classes inclusive of diuretics, is estimated to affect 20-30% of hypertensive patients.[1,2] These patients are more vulnerable to cardiovascular, cerebrovascular and renal complications. The etiology of resistant hypertension is multi factorial but includes both behavioural and biological factors. Patient or clinician-related factors contributing to resistant hypertension include patient's non-adherence to anti hypertensive therapy, White-coat effect and pseudo-hypertension and life style factors (Obesity, alcohol, smoking, dietary sodium etc). Several drugs may induce pre-existing hypertension where non-steroidal anti-inflammatory drugs are usually the most common due to their frequent use; whereas oral contraceptives, sympathomimetics (decongestants, anorectics), adrenal steroids and antineoplastic drugs targeting the vascular endothelial growth factor (VEGF) pathway may contribute to resistant hypertension. Most common secondary causes of resistant hypertension are obstructive sleep apnea, renal artery stenosis, renal parenchymal disease, and primary aldosteronism while some uncommon causes are pheochromocytoma, Cushing's disease, thyroid and parathyroid dysfunction and aortic coarctation. [3,4]

There is convincing evidence that sympathetic nervous system hyperactivity contributes to the initiation, maintenance and progression of hypertension. The renal sympathetic nervous system, in particular, has been identified as a major culprit for the development and progression of hypertension, heart failure and chronic kidney disease in both preclinical and human studies. Traditional surgical sympathectomy proposed in early forties has been discarded due to unacceptable side effects and operative risk. [5-7]

Though compliance has been seriously questioned in such patients yet there are many patients in which in spite of adequate compliance blood pressure does not touch the base line. What are the options for such patients? Up till recently there were hardly any further options for this special class of patients however newer

therapeutic agents and technology offer some hope for such patients. Renal sympathetic denervation has emerged as a new technology which has matured over the last few years and ready to be applied to humans. The rationale is to ablate afferent and efferent sympathetic nerves lining renal arteries by applying different techniques. In animals models nerves have been ablated by applying different toxins from outside and nerves in pelvis have been ablated using electrodes introduced per urethra. In humans electrodes mounted on balloons, baskets and springs have been introduced percutaneously in both renal arteries and utilized to ablate the nerves with gratifying results.[8]

To evaluate the feasibility, efficacy, and safety of catheter-based radiofrequency renal sympathetic denervation for treatment of resistant hypertension, 24 patients with resistant hypertension underwent renal denervation (RDN). The effect on 24-hour ambulatory blood pressure (BP) was assessed at 6 months. RDN was bilateral in 19 patients and single-sided in five. The 19 patients with bilateral RDN showed mean reductions in 24-hour ambulatory BP of 20.7/8.7mm Hg ± 18.1/9.9 (systolic/diastolic; p = .0001/p = .0012). Sixteen bilaterally treated patients (84.2%) showed a systolic BP reduction of at least 10mm Hg and were considered responders, whereas only one of the five patients with single-sided RDN showed a response. Two responders with sleep apnea showed improvement in polysomnography indices, and one with left concentric ventricular hypertrophy showed complete cardiac remodeling 11 months after the RDN procedure. Renal function remained unchanged in all patients, including those with renal failure. Optical coherence tomography of the renal arteries in one patient showed sporadic endothelial scarring. Renal angiograms at 9 months (one patient) and 12 months (two patients) had normal findings. Catheter-based RDN was carried out safely, even in patients with comorbidities, abnormal renal arteries, or anatomic variants.[9]

Renal denervation using the point-by-point application of radiofrequency energy was tested in a prospective, randomised trial, in 106 resistant hypertensive patients at 24 participating centers. Office-based blood pressure measurements in the renal denervation group reduced by 32/12 mm Hg (SD 23/11, baseline of 178/96 mm Hg, p<0·0001), whereas they did not differ from baseline in the control group (change of 1/0 mm Hg [21/10], baseline of 178/97 mm Hg, p=0·77 systolic and p=0·83 diastolic). Between-group differences in blood pressure at 6 months were 33/11 mm Hg (p<0·0001). At 6 months, 41 (84%) of 49 patients who underwent renal denervation had a reduction in systolic blood pressure of 10 mm Hg or more, compared with 18 (35%) of 51 controls (p<0·0001). No serious procedure-related or device-related complications and occurrence of adverse events were noted. This has been shown to reduce blood pressure by 30 mmHg with 85% of patients sustained reduction of 10 mmHg or more till two years after RDN.[10-12]

Recently introduced a balloon-mounted spiral electrode Renal Denervation System with potential to shorten and simplify the procedure was used in a first-in-human study enrolling 9 patients. Baseline BP was 185.67±18.7 mmHg and the reductions at 1, 3, 6 and 12 months were 30.1±13.6 (p=0.0004), 34.2±20.2 (p=0.002), 33.6±32.2 (p=0.021) and 30.6±22.0 (p=0.01 9). No patient developed renal artery stenosis. The OneShot renal denervation system successfully delivered radiofrequency energy to the renal arteries in a short and straightforward procedure.[13]

Percutaneous trans catheter renal sympathetic denervation is proving to be a promising therapeutic option for patients with resistant hypertension. This reduction of blood pressure will result in decrease in number of strokes and myocardial infarction and is anticipated to improve life expectancy. [14] The additional benefits of reducing blood pressure with RDN are shown to be improvement in glycemic control and reversal of left ventricular hypertrophy.[15.16] RDN has also been shown to reduce sleep apnoea, improve renal function and heart failure. [17,18]

To conclude, resistant hypertension is a big challenge considering the high prevalence in middle aged and older population and it claims higher toll in terms of cardiovascular, cerebrovascular and renal complications. Sympathetic renal denervation has proven to be a ray of hope for such patients. It has been shown to reduce blood pressure in short term and confer additional benefits in many studies. The technology has to mature further so that it is available to larger population and at an affordable cost.

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