



## RESISTANT HYPERTENSION

**H**ypertension is defined as systolic pressure of 140 and diastolic pressure of 90 mmHg in patients with age above 18 years. 90-99% patients have essential hypertension.<sup>1</sup> A considerable number of patients do not achieve targeted controlled blood pressure despite life style modifications and medications.

Resistant hypertension is defined as blood pressure that remains above 140/90 mmHg despite use of three antihypertensive medications of different classes at the best tolerated doses, one of which must be a diuretic for at least six months of therapy.<sup>2,3</sup> Approximately 10% patients have resistant hypertension or one in every twenty hypertensive patients.

The etiology is uncertain and multiple factors may be responsible which includes altered renal handling of sodium and water, activation of sympathetic nervous system and genetic factors.<sup>4,5</sup>

Pseudo-resistant hypertension refers to poorly controlled disease which appears resistant but is actually attributable to other factors like non-compliance and insufficient drug therapy.<sup>6</sup>

In resistant hypertension, causes of secondary hypertension like primary hyperaldosteronism, pheochromocytoma, chronic kidney disease, renal artery stenosis and obstructive sleep apnea etc. should be ruled out. Another important factor for resistant hypertension may be non dipping at night or nocturnal hypertension.<sup>7</sup>

The treatment options for resistant hypertension includes ACE inhibitors, ARBs, diuretics, vasodila-

tors like calcium channel blockers or beta blockers and alpha blockers etc.<sup>8</sup> Regarding diuretics, hydrochlorothiazide is more commonly used but chlorthalidone is more potent and have longer half life. Another thiazide like diuretic is indapamide but it has shorter duration of action and can be used in chronic kidney disease. Spironolactone can be added to counteract angiotensin aldosterone system.<sup>9,10</sup>

In beta blockers carvedilol and labetalol are preferred. ON TARGET Trial on use of both ACE inhibitors and ARBs in combination showed no additional benefit.<sup>11</sup>

Two potentially effective interventional therapies are currently being assessed for this purpose. These are renal denervation and carotid sinus stimulation.

Renal denervation is used to ablate sympathetic nerves endings of renal arteries percutaneously. SIMPLICITY HTN 2&3 trials have not shown promising results of renal denervation.<sup>12-13</sup>

The second interventional treatment is carotid sinus stimulation. It is the continuous electrical stimulation of carotid baroreceptors, via an implantable device which inhibits the sympathetic output. The Rheos Pivotal Trial has showed encouraging results but knowledge of device safety and long-term efficacy remains insufficient.<sup>14</sup> So in patients with resistant hypertension, quadruple or five drug approach is recommended. If pharmacological treatment fails then interventional option may be used.

## REFERENCES

1. Murtagh J. North Ryde: McGraw-Hill Australia Pty Ltd; 2011. Murtagh's General Practice.
2. James P, Oparil S, Carter B, Cushman W, Dennison-Himmelfarb C, Handler J, et al. 2014 Evidence-based guidelines for the management of high blood pressure in adults; Report from the panel members appointed to the eighth joint national committee (JNC 8) JAMA. 2014;311:507-20.
3. Pimenta E, Calhoun D. Treatment of resistant hypertension. J Hypertension. 2010;28:2194-5.
4. Persell S. Prevalence of resistant hypertension in the United States, 2003-2008. Hypertension. 2011;57:1076-80.
5. Johnson D. How to treat: Resistant hypertension. Aust Doc. 2007;20:27-34.
6. Moser M, Setaro J. Resistant or Difficult-to-Control Hypertension. N Engl J Med. 2006;355:4. [PubMed] [Google Scholar]
7. Viera A. Resistant hypertension. J Am Board Fam Med. 2012;25:487-95.
8. Frank J. Managing hypertension using combination therapy. Am Fam Phys. 2008;77:1279-86.
9. Kholza N, Chua D, Elliot W, Bakris G. Are chlorthalidone and hydrochlorothiazide equivalent blood-pressure-lowering medications? J Clin Hypertens. 2005;7:354.
10. Friedman O, Logan A. Can nocturnal hypertension predict cardiovascular risk? Integr Blood Press Control. 2009;2:25-37.
11. Mann J, Schmeider R, McQueen M, Dyal L, Schumacher H, Pogue J, et al. Renal outcomes with telmisartan, ramipril, or both, in people at high vascular risk (the ONTARGET study): A multicenter, randomised, double-blind, controlled trial. Lancet. 2008;372:547.
12. Esler M, Krum H, Sobotka P, Schlaich M, Schmeider R, Boehm M, et al. Renal sympathetic denervation in patients with



treatment-resistant hypertension (The SymplicityHTN-2 Trial): A randomised controlled trial. *Lancet*. 2010;376:1903–09.

13. Bhatt D, Kandzari D, O'Neil W, D'Agostino R, Flack J, Katzen B, et al. A controlled trial of renal denervation for resistant hypertension. *N Engl J Med*. 2014;370:1393–401.

14. Bisognano J, Bakris G, Nadim M, Sanchez L, Kroon A, Schafer J, et al. Baroreflex activation therapy lowers blood pressure in patients with resistant hypertension; results from the double blind, randomised, placebo-controlled Rheos Pivotal Trial. *J Am Coll Cardiol*. 2011;58:765–73.

---

**Dr. Muhammad Atif Imran**  
Email: [dratifimran@gmail.com](mailto:dratifimran@gmail.com)

---