CVS CardioVascularServices

Resistant Hypertension: What the General Practitioner Needs to Know

Dr Philip Currie 1/9/2015

Modified from: Resistant Hypertension: What the Cardiologist Needs to Know. *Eur Heart J* 2015 Aug 10

10 key points to remember regarding what a GP needs to know about treatment-resistant hypertension (TRH):

1. The European Society of Hypertension/European Society of Cardiology guidelines on hypertension define TRH as office systolic blood pressure (BP) >140 mm Hg and/or diastolic BP >90 mm Hg despite appropriate lifestyle measures and antihypertensive treatment including a diuretic (at full dose) and two other antihypertensive drugs of different classes at adequate doses. Reported prevalence of TRH varies from 3-30% of hypertensive patients depending on definitions and methods used to measure BP (e.g., office, home, 24-hour ambulatory blood pressure monitoring [ABPM]).

2. 24 hour ABPM is mandatory for the diagnosis, risk stratification, workup in patients with suspected TRH, which by reducing white coat hypertension reduces the prevalence of TRH to <10%. Resistant hypertension by 24-hour ABPM is defined as >130/80 mm Hg, a pulse pressure of >63 mm Hg, or the absence of a night-time drop (dipping of >10% relative to the daytime BP) or the increase of BP during night time (“reverse nocturnal dipping”). Each is often associated with secondary hypertension. When BP is <130/80 mm Hg, the diagnosis is white coat hypertension or inadequate BP technique.

3. Risk factors for resistant hypertension include older age, obesity, diabetes, long duration of hypertension, smoking, and high dietary sodium. Each may be associated with endothelial dysfunction and arterial stiffness, chronic kidney disease, salt sensitivity, and sodium and water retention and volume expansion. The combinations lead to resistant hypertension. When resistant hypertension is documented on 24-hour ABPM, the most common causes of secondary hypertension in the context of treatment resistance and non-dipper status are obstructive sleep apnoea (OSA), renal parenchymal and/or vascular disease, and primary aldosteronism. Screening for each should be considered.

4. Screening for renal parenchymal disease should be performed by urine analysis (protein, erythrocytes, and leucocytes) and measurement of serum creatinine. In the case of a pathological finding, renal ultrasound should be the next step. Although in the general hypertensive population the presence of atherosclerotic renal artery stenosis (RAS) is low (1-8%), its prevalence in patients with TRH is much higher (i.e., 15-40%). Non-dippers with abrupt progression of the severity of hypertension or recent renal function deterioration (particularly after therapy with angiotensin-converting enzyme [ACE] inhibitors or angiotensin-receptor blockers

[ARBs]) or patients presenting with flash pulmonary oedema should be screened for RAS by duplex ultrasound, computed tomography, or magnetic resonance imaging.

5. Primary aldosteronism refers to inappropriately high aldosterone synthesis that is independent of the renin–angiotensin system and cannot be suppressed by sodium loading. Clinical signs of primary aldosteronism are not very specific, and hypokalaemia is present in only about 40%. As a first screening step, the plasma aldosterone–renin ratio (ARR) should be assessed after adequate preparation of the patient. In the case of increased ARR, the patient should be referred to a hypertension specialist for additional workup and treatment.

6. In true TRH vascular remodelling usually results in arterial stiffness. The gold standard to noninvasively assess arterial stiffness is the carotid-femoral pulse-wave velocity or PWV (abnormal >100 m/s). Alternatively, a pulse pressure (systolic BP – diastolic BP) ≥63 mm Hg on 24-hour ABPM suggests increase in stiffness. The absence of increase in arterial stiffness suggests pseudo-resistance related to poor treatment adherence (about one third of suspected TRH), high salt or alcohol intake, decrease in exercise, and drugs interfering with treatment.

7. First steps to hypertension treatment (A+C+D) should include targeting the RAAS activation with an ACE inhibitor or ARB (A); the addition of a dihydropyridine calcium channel blocker (C) or non-dihydropyridine when increased heart rate; and thiazide-like diuretic (D) (chlorthiazide or indapamide). In the elderly and some of African origin, low renin hypertension is common, which may benefit more from sodium depletion than intensified RAAS blockade.

8. If with A+C+D the office BP is >140/90 mm Hg or 24-hour ABPM is >130/80 mm Hg, patients should be assessed for evidence of salt and water retention (oedema, increased sodium excretion, or increased left ventricular [LV] filling pressure), increased sympathetic activation (sympathetic nervous system [SNS] activity) and arterial stiffness by heart rate on 24-hour ABPM and increased pulmonary pressure. In the former, spironolactone (25-50 mg) or eplerenone (50-100 mg) should be added. If not adequate, add a long-acting loop diuretic (i.e., frusemide) to the thiazide. In case of increased SNS activity or arterial stiffness, an alpha blocker (i.e., doxazosin) or if needed a beta-blocker with vasodilator properties (carvedilol, or labetalol).

9. Patients with TRH are at high risk for cardiovascular morbidity and mortality and should be screened for target organ damage. Examples include echo evidence of LV hypertrophy (≥115 g/m ^{2} in men and ≥95 g/m^2 in women), left atrial area ≥34 ml/m^2, enlarged aorta, LV ejection fraction <55%, and altered LV filling pressure with transmitral E/e' ≥13.

10. If patients with TRH report symptoms evoking generalized arteriosclerosis (i.e., angina pectoris, claudication, and cerebrovascular symptoms) and/or the physical examination reveals suspicious signs, rapid diagnostic workup (i.e., coronary angiography and duplex of cerebral and peripheral arteries) should be performed, because TRH increases the risk for cardiovascular disease, and if associated with coronary artery disease, it markedly increases cardiovascular morbidity and mortality.