

Hypertension and the kidney

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INTRODUCTION

The reduction in myocardial infarctions and strokes seen with antihypertensive therapy is not matched by a decline in renal failure. In fact, there seems to be a steady increase in end-stage renal failure, more so in black patients.¹ Available evidence strongly suggests that in patients with hypertension, even minor abnormalities of renal function, predicts a worse cardiovascular outcome.² Mild to moderate renal insufficiency in patients with essential hypertension is due to an expression of renal microvasculopathy (pre-glomerular arteriolar arteriosclerosis and tubulo-interstitial changes). The microangiopathy may be triggered by: (a) sympathetic overactivity; (b) over stimulated renin-angiotensin system; or (c) any other factor that causes renal vasoconstriction.³

HYPERTENSION AND THE KIDNEY

a. Renal contribution to essential hypertension:

Essential hypertension caused by the kidney may play a role in the development of salt sensitivity and may even have an influence on peripheral vascular resistance.

b. Hypertension as a cause of renal dysfunction:

(Vascular Pathology)

i. Atherosclerosis:

Hypertension is a risk factor for atherosclerosis and cardiovascular disease. Atherosclerosis of the abdominal aorta and renal arteries may also cause hypertension.

ii. Degenerative changes:

Large and medium arteries are affected and lead to:

- Aortic dissection. (Blood pressure may suddenly rise during acute dissection)
- Cerebrovascular haemorrhage

iii. Small blood vessel disease:

Hyaline arteriosclerosis:

Homogenous pink hyaline thickening of walls of arteries (with luminal narrowing). This is seen in:

- Hypertension (characteristic of benign nephrosclerosis)
- Old age
- Diabetes Mellitus (more segmental changes)

Lesions reflect leakage of plasma components across vascular endothelium and excessive extracellular matrix production by smooth muscle cells (SMC). These small blood vessels changes are seen mainly in the afferent arterioli of the kidney.

Hypertensive nephrosclerosis:

- GFR < 60 ml/min (clinically diagnosed as a reduction in creatinine clearance)
- Urine protein > 150 mg/24 hr.⁴

Microalbuminuria: 24 Hour excretion of albumin of between 30 and 300 g indicates an early lesion. This early lesion can predict an increased cardiovascular risk and may predict the development of end stage renal disease. These small blood vessel changes lead to endstage renal failure.

Hyperplastic arteriosclerosis:

Onion-skin, concentric, laminated thickening of walls of arteries (with narrowing of lumen). The laminations are due to SMC and thickened and reduplicated basement membranes. This lesion is typical of malignant hypertension and in addition there are also fibrinoid deposits and acute necrosis of vessel wall (= necrotising arteriolitis).

c. Renal parenchymal hypertension:

Chronic renal failure is a common cause

of secondary hypertension and is a major risk factor for the morbidity and mortality in patients with chronic renal failure.

d. Renovascular hypertension:

The main cause of renal artery stenosis is atherosclerosis (± 90% of cases), typically in older patients with other manifestations of atherosclerosis and fibromuscular dysplasia (± 10% of cases), and in women between 15 and 50 years of age.

GOAL BLOOD PRESSURE FOR HYPERTENSIVE PATIENTS ON TREATMENT

- **Low-risk hypertensives:** No target organ damage (TOD), no clinical cardiovascular (CV) disease; at least one CV risk factor, excluding DM: **BP < 140/90 mmHg.**
- **High-risk hypertension:** TOD; clinical CV disease: **BP 130/80 mmHg.**
- **Diabetes Mellitus:** All type 2 diabetics and type 1 diabetics with microalbuminuria: **BP 130/80 mmHg.**
- **Renal disease:** **BP 130/80 mmHg.**
- **Proteinuria > 1 g/24 hrs:** **BP < 125/75 mmHg.**

HOW TO ACHIEVE GOAL BLOOD PRESSURE:

- Majority of patients will require a combination of lifestyle modifications and more than one drug.
- All the major antihypertensive classes can be used as initial drugs: diuretics, beta-blockers, calcium channel antagonists, ACE-inhibitors, and angiotensin receptor blockers (ARB). However, ACE-inhibitors and ARB's are preferred in renal disease/diabetics.
- Low-dose thiazides should ideally be part of any combination.

SPECIFIC ISSUES IN TREATMENT OF KIDNEY DISEASE/DIABETES:

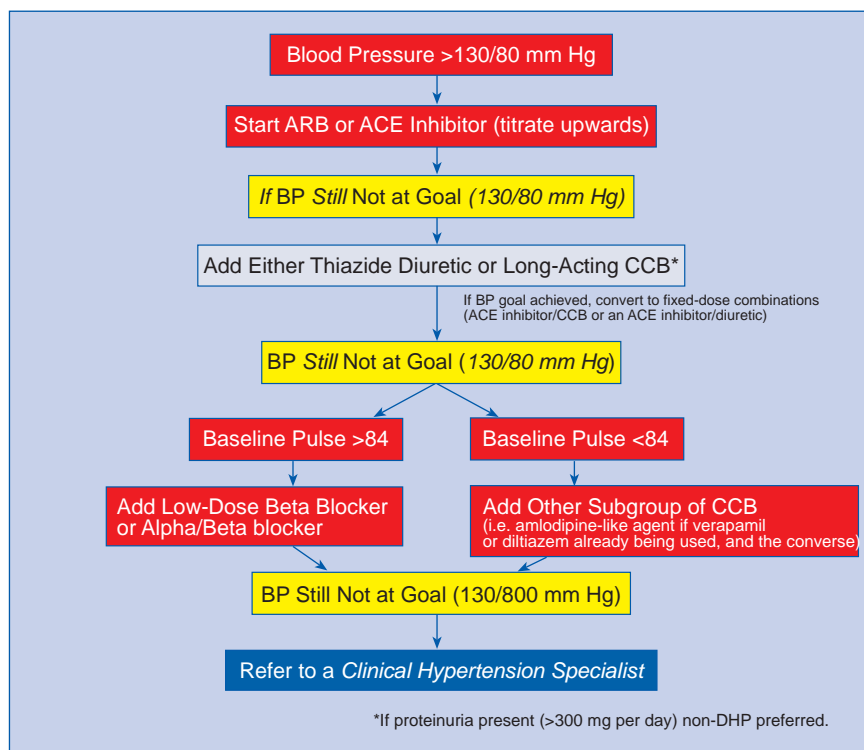
1. Target blood pressure on treatment:^{5,6} **BP 130/80 mmHg.**

- Drugs that inhibit the *renin-angiotensin system* should be a prominent part in therapy as they:
 - Reduce proteinuria
 - Reduce risk of reaching end-stage renal disease (ESRD) and can postpone ESRD
- See algorithm for achieving target BP goals in those with diabetes or renal insufficiency.✎

See CPD Questionnaire p.53

References

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Press Release

TEVETEN® (EPROSARTAN) REDUCES FUTURE RISK IN HYPERTENSIVE STROKE PATIENTS

The established antihypertensive agent TEVETEN® (eprosartan) has now been shown to offer effective protection against cerebrovascular and cardiovascular events in hypertensive patients with a previous stroke, over and above that offered by blood pressure reduction.

Initial results from the landmark MOSES* study, presented by Professor Joachim Schrader at the XXVI Congress of the European Society of Cardiology in Munich, showed that blood pressure was equally well controlled when hypertensive patients with a history of stroke were treated with either TEVETEN®-based or nitrendipine-based therapies. However, there was a significant reduction of 20% in the primary endpoint (total mortality and total cardiovascular and cerebrovascular events) in the TEVETEN® group. In addition, there was a significant reduction of 25% in the recurrence of stroke and associated disease (transient ischaemic attack [TIA] and prolonged reversible neurological ischaemic deficit [PRIND]), and a significant reduction of 30% in first-time cardiovascular events in patients treated with TEVETEN®.

TEVETEN® is a member of the class of drugs known as angiotensin-II receptor antagonists, which target the renin-angiotensin-aldosterone system. Other drugs from this class have previously demonstrated cardio- and cerebroprotective effects in patients at risk of stroke. However, earlier studies focused on patients who, although at risk, have not yet had a stroke. These studies helped to establish the value of antihypertensive treatment in primary stroke prevention, but until now there were few data on the effectiveness of these drugs in preventing recurrent stroke.

MOSES is the first study to specifically compare the outcomes of alternative antihypertensive treatment in patients with a history of stroke. The calcium channel blocker nitrendipine was chosen as the comparator agent because of its success in the Syst-Eur study,¹ where treatment reduced the risk of stroke by 42% in elderly patients with systolic hypertension. In the MOSES study, both nitrendipine and TEVETEN® produced impressive reductions in blood pressure, with approximately 75% of patients in each

group reaching the target blood pressure as determined by ambulatory blood pressure monitoring. Since both agents produced similar reductions in blood pressure, the reduced incidence of cerebrovascular and cardiovascular events in patients receiving TEVETEN® indicates that these benefits are achieved independently of blood pressure reductions.

Throughout the world, over 20 million people each year suffer a stroke. Approximately 25% of strokes are fatal but among the 75% who survive, stroke is a cause of considerable disability. Many patients never recover full function and become dependent on others for help with everyday living. They are also at high risk of suffering a further stroke – compared with the population as a whole, their risk of stroke is multiplied 1.5-fold. A second stroke may be truly devastating.

MOSES has now demonstrated the efficacy of TEVETEN® in reducing the incidence of recurrent stroke-related disease. These results may therefore have significant implications for the choice of antihypertensive prescribed for these patients.

For further medical information, please visit www.moses-study.com

*Morbidity and Mortality after Stroke – Eprosartan compared with nitrendipine for Secondary prevention. References

Reference

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