Treating hypertension today

**KEY MESSAGES**

- Lifelong hypertension management should not be based on a single or two blood pressure measurements.
- Technology, at modest cost, offers the opportunity to optimise the clinical measurement of blood pressure.
- Out-of-office blood pressure measurement is changing the landscape of treatment.
- Hypertension is a complex disorder requiring a rigorous approach to treatment.
- When we choose antihypertensive agents, we must ensure 24-hour coverage.
- Hypertension is also a small-vessel disease and autoregulation is critically important.
- Large-vessel stiffening is very important in the elderly and complicates treatment.

We need to take control of the epidemic of hypertension in South Africa because it is responsible for significant numbers of deaths in our economically active population. Our mortality from hypertension is three times that of the USA. Treating hypertension is highly cost effective and provides unquestionable benefits,” Professor Brian Rayner stressed in his review of issues in hypertension in 2014 at the recent Cape Town Congress of the Faculty of Consulting Physicians.

In South Africa, funders are too active in dictating the selection of hypertensive therapy in the private sector. “The public sector in South Africa is ahead of the private sector in terms of the choice of antihypertensive agents available to clinicians,” Professor Rayner noted.

What do we mean by hypertension?

Conceptually, the following definitions can be useful in understanding and treating hypertension:

- Hypertension is a progressive cardiovascular syndrome arising from complex and interrelated aetiologies.
- Early markers of the syndrome are present before blood pressure elevation is observed.
- Progression is strongly associated with functional and structural cardiac and vascular abnormalities that damage heart, brain and vasculature and other organs. This in turn leads to premature morbidity and death.¹

Based on the above, a hypertension diagnosis should not be made further to a single blood pressure measurement taken in a doctor’s office/clinic. “Nor can we base it on the classic definition of hypertension as taught in medical schools over the past decades (Table 1).”

The inadequacies of a single office blood pressure measurement are highlighted by our current understanding of blood pressure variability and the fact that both low diastolic blood pressure and nocturnal blood pressure are predictors of mortality. “Augmentation of systolic blood pressure occurs with ageing and is adversely affected by stiffening of the arteries,” Professor Rayner pointed out.

Newer technologies, such as ambulatory blood pressure monitoring (ABPM), new devices to measure central aortic blood pressure and automated office machines (e.g. the devices from Omron) that take six readings at two-minute intervals, allow the clinician to get a better overall view of hypertension in the individual patient. “One or two blood pressure

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**Table 1. Definition of hypertension in patients over 18 years**

<table>
<thead>
<tr>
<th>Category</th>
<th>Blood pressure, mmHg</th>
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<tbody>
<tr>
<td></td>
<td>Systolic</td>
</tr>
<tr>
<td>Optimal &lt;120</td>
<td>and</td>
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<tr>
<td>Normal &lt;130</td>
<td>and</td>
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<tr>
<td>High-normal</td>
<td>130 – 139</td>
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Hypertension

<table>
<thead>
<tr>
<th>Stage</th>
<th>Blood pressure, mmHg</th>
<th>Stage</th>
<th>Blood pressure, mmHg</th>
<th>Stage</th>
<th>Blood pressure, mmHg</th>
</tr>
</thead>
<tbody>
<tr>
<td>Stage 1</td>
<td>140 – 159</td>
<td>and/or 90 – 99</td>
<td>Stage 2</td>
<td>160 – 179</td>
<td>and/or 100 – 109</td>
</tr>
<tr>
<td>Stage 3</td>
<td>180</td>
<td>and/or 110</td>
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One or two blood pressure readings are not a good basis for deciding on chronic lifelong antihypertensive medication. “If blood pressure is high (>180/110mmHg) then treatment is needed without further measurement, but if systolic blood pressure is 140-160mmHg in patients without target organ disease, then ABPM is mandatory in my view,” Professor Rayner said.

Clinical learnings from new technologies

The extreme dipper on ABPM

“The phenomenon of ‘extreme dipping’ is frequently seen when ABPM readings are done in an older patient, with extreme drops in blood pressure at night and a predominantly high, but highly variable, blood pressure during the day (Figure 1).

“A picture like this is common in the aged hypertensive with stiff arteries – when we see this we should be thinking, ‘These patients are their brain!’ If an MRI is done, it may well show the white spots of silent cerebral ischaemia. This is borne out by research done on the ‘dipper phenomenon’ (Figure 2).”

Masked hypertension – what is it and how do we recognise masking?

Masked hypertension is a real entity. Research has shown that these patients, if left untreated, have the worst outcomes. The diagnosis of masking can be aided by three scenarios:

1. Normal office blood pressure but patient still has significant target organ damage (e.g. abnormal left ventricular hypertrophy (LVH) on ECG), which is not resolving, despite blood pressure being controlled.
“As physicians, we need to take hypertension seriously, see patients frequently to endorse this attitude and use appropriate technology to monitor patients’ progress.”

Professor Brian Rayner

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2. Higher out-of-office blood pressure readings, e.g. at the pharmacy.
3. Treatment in the modern era must be based on self, automated or ambulatory monitoring.

“Using these modalities entails the use of different cut-off norms. I use the automated office system - six readings every two minutes - discarding the first and calculating the mean of the rest. If done by the nurse, this can also help to reduce white coat hypertension,” Professor Rayner said (Table 2).

### Loss of autoregulation and damage to brain, kidneys, heart and eyes

“We know that hypertension is a risk factor for atherosclerosis, but a lot of hypertension-related damage occurs in the microvascular system of the kidney, brain and eye.” Ageing and diabetes result in the loss of autoregulation; in diabetics, in particular, the kidneys are extremely vulnerable (Figure 3).

The loss of autoregulation results in endothelial injury, increased vascular permeability, cell proliferation, activation of platelets and coagulation, activation of the renin-angiotensin-aldosterone system (RAAS) – with low potassium levels, often the hallmark of malignant hypertension. This can result in stroke, hypertensive nephrosclerosis, LVH and retinal damage.

### Lifestyle issues in hypertension

Lifestyle is critically important. The South African Hypertension Society advocates the DASH diet, which is high in fruit and vegetables with a lowered intake of saturated fat. Weight loss is crucial. Reducing salt intake, also at a population level, is a useful additional strategy to lower blood pressure across the board.

“As physicians, we need to take hypertension seriously, see patients frequently to endorse this attitude and use appropriate technology to monitor patients’ progress,” Professor Rayner concluded.
Adherence to therapy

Adherence to hypertension therapy is generally poor. A recent study showed that within one year about 50% of patients had stopped taking their medication. Among those who continued to take their medication, about 30% of these patients were not taking their medication correctly and were having drug holidays of at least four days (Figure 4). “Patients fiddle with their medication and single pills delivering two antihypertensive drugs reduce this complicating factor,” Professor Rayner noted.

Compliance with therapy and persistence are improved when fixed-dose combinations are used (Figure 5).
Efficacy of fixed-dose combinations

One of the key studies of free versus fixed-dose combinations was ACCOMPLISH. It involved patients at very high risk of cardiovascular events, including diabetics. It showed that initiation of therapy with a fixed-dose of benazapril/amlopidine in a single pill achieved target blood pressure control in 70% of patients as compared to the 30% control achieved with forced titration using the combination of benazapril and hydrochlorothiazide, also initiated as a single pill.8 (Table 3)

A retrospective evaluation of the outcomes of patients treated from the outset with a fixed-drug combination compared to similar patients treated with monotherapy and later switched to combination therapy provides a real world view of the consequences of these two different approaches (Figure 6). Although not a prospective randomised trial, the results are interesting and show that the initial combination therapy was associated with a significant reduction in the risk of cardiovascular events or death. This was found to be primarily due to the rapid achievement of target blood pressure."

Table 3. Summary of the advantages of early use of a fixed-dose combination

<table>
<thead>
<tr>
<th>Advantage</th>
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<tr>
<td>Achieves better blood pressure control, particularly if synergistic physiological actions are chosen, e.g. low-dose thiazides and RAS blocker; ACE-inhibitor and CCB</td>
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<tr>
<td>Achieves earlier blood pressure control</td>
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<tr>
<td>Fewer traditional side-effects</td>
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<tr>
<td>Fewer withdrawals from medication</td>
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<tr>
<td>Improved patient compliance</td>
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Footnote: Key summary by Professor Brian Rayner

Figure 6. Incidence rates and incidence rate ratios of cardiovascular (CV) events

Which combination therapy?

“In South Africa, thiazide and thiazide-like diuretics still have a place in the management of blood pressure, but low-dose thiazides should generally be used. In addition, we really do need a study of indapamide and chlorthalidone in our black African population,” Professor Rayner noted.

“The ASCOT-BPLA study is a landmark
trial that changed clinical practice. It showed the value of a CCB/ACE-inhibitor approach in patients at high risk of cardiovascular events as compared to an atenolol/thiazide combination.

“All-cause mortality risk was reduced (11%) in the ASCOT study and the cardiovascular mortality risk significantly reduced in those receiving the CCB ± ACE-inhibitor combination, despite a small difference in blood pressure in the two treatment arms (2mmHg).” There has been much discussion about the reasons for these significant outcome benefits with amlodipine ± perindopril. We now believe it is likely to be due to better nocturnal blood pressure lowering and less visit-to-visit and within-visit variability, factors which are now known to be associated with improved outcomes,” Professor Rayner concluded.

Conflict of interest:
Received speaker honoraria from Novartis, Servier, Bayer, Sanofi, Boehringer Ingelheim, MSD and Merck.

References: