



Cardiology

Hypertension Module 144: August 2009



Prescribing blood pressure-lowering drugs for patients with hypertension will only prevent the cardiovascular consequences of hypertension if blood pressure control is achieved

(This module was facilitated by Prof Eoin O'Brien)

STROKE AND COGNITIVE IMPAIRMENT constitute a major economic and societal burden in Ireland. Ireland is being swept along in the global epidemic of hypertension. Worldwide, the estimated number of adults with hypertension was 972 million in 2000; by 2025, the total number is expected to increase to 1.56 billion.¹ Poor control of high blood pressure is now recognised as the major cause of stroke – the most catastrophic consequence of hypertension.¹⁻³

However, recently the role of poorly controlled blood pressure in the elderly has been shown to be a major cause of cognitive impairment leading ultimately to dementia in the older population.^{4,5} Elevated blood pressure is the most significant factor in causing deterioration of performance in the ageing brain, and reduction of blood pressure to normal levels in the elderly would reverse cognitive impairment and prevent stroke, which are rightly looked upon with dread by ageing members of society and their families.

Over the past decade there have been some 85,000 strokes in Ireland. Stroke is the third most common cause of death in Ireland. Approximately 10,000 acute strokes are admitted to hospital in the Republic of Ireland each year and of these, 30% die within one year. Approximately 2,000 people die from stroke each year accounting for more deaths than breast cancer, lung cancer and bowel cancer combined.

For those who survive – some 30,000 people – only half make a complete recovery, leaving the remainder with the problems of coping with serious disability and in need of support to cope with the activities of daily life – all of which places a severe burden on the health services and causes immense distress to the victims of stroke and their families.^{6,7}

In midlife age groups, the presence of elevated systolic blood pressure accounts for up to 11% of the variance in cognitive performance, which suggests that in community-dwelling hypertensive individuals who do not have overt dementia, elevated blood pressure may account for one-tenth of cognitive impairment and thus for an increased risk for dementia.⁵

Moreover, cognitive impairment may also be associated with excessive lowering of blood pressure in the elderly, an occurrence that makes it essential to ensure that treatment gives smooth reduction of pressure over 24-hours without excessive lowering leading to hypotension.^{8,9}

Increased longevity

As the age of the Irish population increases, the prevalence of these conditions is rising. In Ireland, high blood pressure affects more than 50% of the population over the age of 60 years; this rises to 70% in those aged 70 years and over. Less than 40% will have adequate control of blood pressure over 24 hours.¹⁰⁻¹²

If high blood pressure was properly controlled, stroke would be reduced by at least 50%¹³ and it can be reasoned that cognitive impairment could be ameliorated leading to a reduction in the onset of dementia. (*See Table 1 for initiation of antihypertensive treatment*).

Control of blood pressure

There is a large range of drugs available for the effective lowering of blood pressure, yet in real life only about one-third of people with high blood pressure in Ireland are known to be adequately controlled despite having medication prescribed.^{13,14}

Lack of blood pressure control is the main cause for the unacceptable increase in stroke and cognitive impairment in the ageing population. Part of the problem is that patients do not appreciate the need to continue taking medication in the mistaken belief that hypertension is a disease that can be cured, and they stop or reduce medication when blood pressure levels fall.

As a *Lancet* editorial put it recently: “Physicians need to convey the message that hypertension is the first, and easily measurable, irreversible sign that many organs in the body are under attack.”¹¹

Elevation of blood pressure, though only one component of a number of risk factors that may affect the ageing brain (others being smoking, excessive salt, elevated cholesterol,



Table 1

| Initiation of antihypertensive treatment | | | | | |
|--|--|--|--|---|--|
| Blood pressure (mmHg) | | | | | |
| Other risk factors, OD or disease | Normal SBP 120-129 or DBP 80-84 | High normal SBP 130-139 or DBP 85-89 | Grade 1 HT SBP 140-159 or DBP 90-99 | Grade 2 HT SBP 160-179 or DBP 100-109 | Grade 3 HT SBP ≥ 180 or DBP ≥ 110 |
| No other risk factors | No BP intervention | No BP intervention | Lifestyle changes for several months, then drug treatment if BP uncontrolled | Lifestyle changes for several weeks, then drug treatment if BP uncontrolled | Lifestyle changes and immediate drug treatment |
| One to two risk factors | Lifestyle changes | Lifestyle changes | Lifestyle changes for several weeks, then drug treatment if BP uncontrolled | Lifestyle changes for several weeks, then drug treatment if BP uncontrolled | Lifestyle changes and immediate drug treatment |
| Three or more risk factors, MS or OD | Lifestyle changes | Lifestyle changes and consider drug treatment | Lifestyle changes and drug treatment | Lifestyle changes and drug treatment | Lifestyle changes and immediate drug treatment |
| Diabetes | Lifestyle changes | Lifestyle changes and drug treatment | | | |
| Established CV or renal disease | Lifestyle changes and immediate drug treatment | Lifestyle changes and immediate drug treatment | Lifestyle changes and immediate drug treatment | Lifestyle changes and immediate drug treatment | Lifestyle changes and immediate drug treatment |

Adapted from: 2007 Guidelines for the management of arterial hypertension. The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). Eur Heart J 2007; 28: 1462-1536

diabetes and obesity), is the single most important risk contributing to 60% of all cardiovascular deaths.¹⁵

Recent evidence shows that although prescribing of blood pressure-lowering drugs has increased, blood pressure control has not improved. It is now known that prescribing alone is not the answer – the drugs prescribed must bring blood pressure down to normal not only during the day but also at night.¹⁶

Importance of blood pressure control

There can be no dispute about the benefit of blood pressure-lowering. Improved blood pressure control in the elderly could have a major impact on the quality of life by preventing cognitive impairment and prevention of debilitating incapacity as a result of stroke and dementia. The viewpoint once expressed that hypertension is an inevitable consequence of the ageing process that should, therefore, be left untreated, especially in the very elderly, has been finally shown to be scientifically untenable, with recent evidence showing that even treating people older than 80 years reduces cardiovascular mortality.¹⁷

A meta-analysis of eight placebo-controlled trials in 15,693 elderly patients followed for four years showed that active antihypertensive treatment reduced coronary events by 23%, strokes by 30%, cardiovascular deaths by 18%, and total deaths by 13%, with the benefit being greatest in patients older than 70 years.¹⁸ However, ‘treatment’ is more

than merely prescribing drugs.

Hypertensive patients in whom blood pressure is uncontrolled by treatment have a cardiovascular risk only modestly less than that of untreated individuals,¹⁹ which leads to the conclusion that in practice, blood pressure-lowering drugs are prescribed inappropriately without achieving optimal control, or put another way “patients are frequently not barely but badly controlled”.¹⁶

This therapeutic inertia whereby the prescribing of medication is seen as constituting an end in itself in that some good will be achieved must now be replaced by a clinical modus operandi recognising that the efficacy of medication will ultimately determine the fate of the patient with hypertension (see Table 2 for preferred drugs in antihypertensive treatment).

Efficacy, however, can only be gauged by the achievement of evidence-based target levels of blood pressure, which in turn demands accurate measurement of blood pressure that should also be capable of indicating that treatment is resulting in control over the 24-hour period.³

Measurement of blood pressure

One of the most important explanations for the failure of medical management is that the technique of blood pressure measurement used in practice (which is over 100 years old) is inaccurate and cannot give an estimate of blood pressure control over 24 hours.



Table 2

Antihypertensive treatment: preferred drugs

The presence of subclinical organ damage, clinical cardiovascular disease, renal disease or diabetes may be more favourably treated by some drugs than others

Subclinical organ damage

| | |
|------------------------------|--|
| LVH | ACE inhibitor, calcium antagonists, angiotensin receptor antagonists |
| Asymptomatic atherosclerosis | Calcium antagonists, ACE inhibitor |
| Microalbuminuria | ACE inhibitor, angiotensin receptor antagonists |
| Renal dysfunction | ACE inhibitor, angiotensin receptor antagonists |

Clinical event

| | |
|-------------------------------|---|
| Previous stroke | Any BP lowering agent |
| Previous MI | Beta-blockers, ACE inhibitor, angiotensin receptor antagonists |
| Angina pectoris | Beta-blockers, calcium antagonists |
| Heart failure | Diuretics, beta-blockers, ACE inhibitor, angiotensin receptor antagonists, antialdosterone agents |
| Recurrent atrial fibrillation | Angiotensin receptor antagonists, ACE inhibitor |
| Permanent atrial fibrillation | Beta-blockers, non-dihydropyridine calcium antagonists |
| Renal failure/proteinuria | ACE inhibitor, angiotensin receptor antagonists, loop diuretics |
| Peripheral artery disease | Calcium antagonists |

Condition

| | |
|--|--|
| Isolated systolic hypertension (elderly) | Diuretics, calcium antagonists |
| Metabolic syndrome | ACE inhibitor, angiotensin receptor antagonists, calcium antagonists |
| Diabetes mellitus | ACE inhibitor, angiotensin receptor antagonists |
| Pregnancy | Calcium antagonists, methyldopa, beta-blockers |
| Blacks | Diuretics, calcium antagonists |

Adapted from: 2007 Guidelines for the management of arterial hypertension. The Task Force for the Management of Arterial Hypertension of the European Society of Hypertension (ESH) and of the European Society of Cardiology (ESC). Eur Heart J 2007; 28: 1462-1536

A number of studies have now clearly demonstrated that nocturnal hypertension is a major risk for the development of stroke and other cardiovascular events.²⁰ There is also evidence that night-time blood pressure may be an important determinant of cognitive impairment.²¹ This important component of the 24-hour blood pressure profile can only be measured by ambulatory blood pressure measurement (ABPM), which provides the profile of blood pressure not only during the day but also at night.³

It has been estimated that the conventional technique of measurement used in most general practices today is leading to incorrect readings in as many as a third of all patients attending for routine blood pressure measurement.²² It follows, therefore, that assessing blood pressure control is seriously flawed and moreover the technique does not allow the response to treatment to be assessed over the 24-hour period.

Because of this and the proven cost-effectiveness of the technique,²³ clinical use of ABPM has been increasing rapidly throughout the world,²⁴ but its availability to patients with high blood pressure in the Irish community remains low and much under-utilised. With conventional measurement, the doctor is provided with only one, or at best, a few measurements, obtained under artificial circumstances that are subject to the white coat reaction and which bear no relationship to the variability of blood pressure over the 24-hour period.

On the other hand, ABPM provides detailed information of an individual's blood pressure response in the medical environment while the device is being fitted during the first hour – the white coat window, during daytime activity,

during sleep and in the matinal window before awakening when extreme rises in blood pressure may herald the onset of stroke.²⁵

In the light of the evidence available on the societal and financial consequences of uncontrolled hypertension, the cost of equipment becomes relatively insignificant; every patient suspected of having hypertension should have ABPM to confirm or refute the diagnosis, and every patient with uncontrolled hypertension should have ABPM repeated as necessary until 24-hour control of blood pressure is achieved.²²

ABPM in primary care

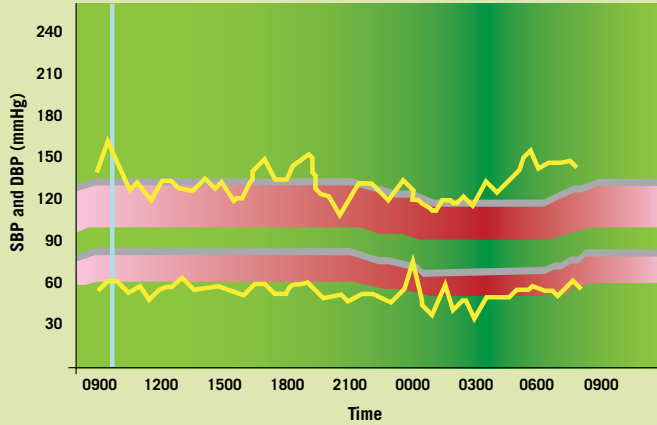
ABPM is a feasible, albeit underused technique in primary care. One of the first studies of ABPM in primary care – the RAMBLER I study – performed primarily in Ireland, showed that only 12% of patients achieved target blood pressure with conventional office measurement compared to over one-third of patients with ABPM. Furthermore 38% of patients had a change in their medication as a result of ABPM; 32% had a new medication started and 14% of untreated patients with elevated office blood pressure, who were candidates for drug treatment, were not commenced on medication because ABPM was normal.²⁶

The largest study to date on ABPM in primary care comes from Spain where a nationwide project to promote the use of ABPM in primary care settings is being established. In this large cohort of some 20,000 patients, office blood pressures were approximately 16/9mmHg higher than ABPM in patients categorised as being at low to moderate added risk with a greater difference (23/23mmHg) in those

Table 3

Examples of dabl interpretative report and trend report

24-hour ambulatory blood pressure measurement report for a male patient

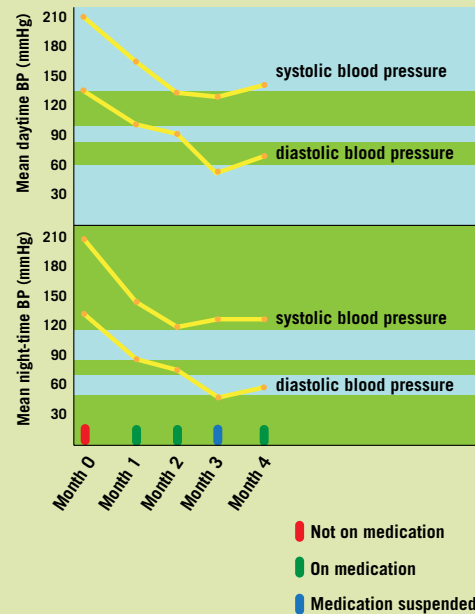


dabl@ assessment

The ABPM suggests normal daytime systolic blood pressure (130mmHg), mild night-time isolated systolic hypertension (126mmHg) and low 24-hour diastolic blood pressure (55mmHg daytime, 48mmHg night-time) with a whitecoat effect (159mmHg/61mmHg)

These reports are adapted from examples of dabl@ reports 2009

Mean ABPM blood pressure trend report for a male patient over a five-month period



categorised as being at high risk in spite of receiving much more antihypertensive treatment.

Moreover, high-risk hypertensive patients showed a high prevalence of circadian rhythm abnormalities on ABPM with the prevalence of a non-dipping pattern being almost 60%, and in patients with the lowest ABPM levels, high-risk patients showed a higher prevalence of non-dipping nocturnal BP than lower-risk cases. An editorial commentary on this study urges the wider use of ABPM to gain more accurate risk categorisation of patients in the community as well as being able to obtain a more accurate estimate of the community control of blood pressure.

As in the Irish study, blood pressure control was better when assessed by ABPM than by office blood pressures indicating that the white coat effect with office blood pressure is leading to an underestimation of blood pressure control in the community.

Blood pressure control was underestimated in over a third of patients and overestimated in some 5% by office blood pressure as compared to ABPM. Notably, blood pressure was uncontrolled by both methods of measurement in 43% of patients. High-risk patients showed poorer ABPM control than low-to-moderate risk patients in spite of receiving much more antihypertensive treatment.¹⁰⁻¹²

RAMBLER II study

Until recently, the interpretation of ABPM was complex because computerised techniques and electronic transmission of data were not utilised to make the procedure more accessible to doctors and their patients. The dabl ABPM system used in the RAMBLER I has been developed to provide a number of facilities that will be utilised in

the RAMBLER II study (see Table 3 for examples of dabl reports).^{3,27}

Conclusion

Longevity in Ireland, as in other developed countries, is rising due mainly to improved medical and surgical management of the consequences of cardiovascular disease which in earlier generations caused premature death. The greatest threat to the growing elderly population is elevated blood pressure, which affects some 60-70% of elderly citizens.

However, despite having an array of drugs capable of achieving effective blood pressure-lowering, the reality is that less than half of patients with hypertension have adequate control of blood pressure.

The major consequences of uncontrolled blood pressure in the elderly are cognitive impairment and stroke. It is estimated that if blood pressure was controlled in Ireland, some 5,000 strokes could be prevented annually. The level of blood pressure control in the Irish population is worsening rather than improving and if increased longevity is not to be blighted by disability, innovative efforts to achieve blood pressure control must be initiated. Previous practice methods have clearly failed. Utilising ABPM linked to electronic technology provides an innovative approach based on sound evidence, which can alter the outlook for the aged by protecting the ageing brain from the cardiovascular consequences of uncontrolled hypertension.

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References on request