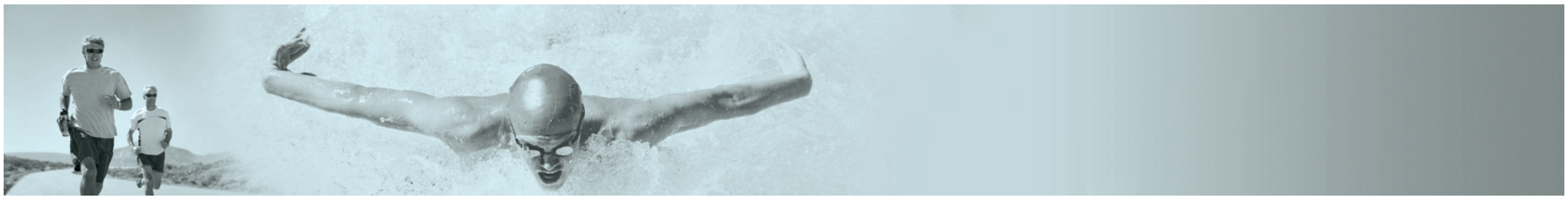

Blood pressure measurement

Clinical developments in hypertension management

Prof Eoin O'Brien outlines the benefits of ambulatory blood pressure management and looks at the development of the 'flexipill' as the next generation of drug treatment

The technique for measuring blood pressure was introduced into clinical medicine in 1896 and has survived largely unchanged for over a century, despite being inherently inaccurate. These concerns have resulted in considerable research into techniques for assessing blood pressure away from the medical environment, foremost amongst which has been ambulatory blood pressure measurement (ABPM).

Indeed, this technique is now accepted as being indispensable to good clinical practice. There are guidelines and recommendations laying down the criteria for validation of devices for ABPM and the website www.dableducational.org provides up-to-date information on recommended devices.

The advantages for ABPM are many. The technique gives more measurements than conventional measurement, and the real blood pressure is reflected more accurately by repeated measurements [Fig 1]. ABPM provides a profile of blood pressure away from the medical environment, thereby allowing identification of individuals with a 'white coat' response [Fig 2], or masked hypertension, who are in need of careful management. ABPM shows blood pressure behaviour over a 24-hour period rather than giving a snapshot of blood pressure performed with an inaccurate technique under artificial circumstances, so that the efficacy of antihypertensive medication over a 24-hour period becomes apparent rather than relying on one or a few conventional measurements confined to a short period of the diurnal cycle. ABPM can identify patients with abnormal patterns of nocturnal blood pressure, such as non-dippers [Fig 3].

Finally and importantly, evidence is now available from longitudinal studies that ABPM is a much stronger predictor of cardiovascular morbidity and mortality than conventional measurement.

Importance of nocturnal blood pressure

I first introduced the 'dipper/non-dipper' classification in 1988 when a retrospective analysis suggested that non-dipping hypertensive patients had a higher risk of stroke than the majority of patients with a dipping pattern. It is now accepted that a diminished nocturnal blood pressure fall is associated with a poor prognosis.

Moreover, nocturnal blood pressure is now known to be an independent risk for cardiovascular outcome over and above all other measures of blood pressure. For example, in the Dublin Outcome Study, for each 10-mm Hg increase in mean nighttime systolic blood pressure, the mortality risk increased by 21 per cent. Cardiovascular events such as myocardial infarction, ischaemia and stroke are more frequent in the morning hours, soon after waking, than at other times of day.

In older hypertensive subjects, a morning surge in blood pressure — defined as a rise in blood pressure >55 mm Hg from the lowest night-time reading — carries a risk of stoke almost three times greater than that seen in patients without a morning surge.

Availability of ABPM

ABPM is used extensively in primary care in Ireland. In fact, figures suggest that the technique is used more frequently in Ireland than in the UK and the availability of the dabl system for on-line hosting and transmission of a one-page interpretative report with the facility to plot trends is greatly facilitating the availability of ABPM in primary care [Fig 4].

The RAMBLER II study, which has enrolled over 200 practices across the country, shows the willingness of general practitioners to adopt the methodology of ABPM. However, reimbursement for the technology should be provided to make the technique widely available in primary care.

ABPM is also being provided in pharmacies and this is proving a popular means of making the technique more widely available to patients with hypertension.

Importance of blood pressure control

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. 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.

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

Recent evidence shows that although prescribing of blood pressure-lowering drugs has increased, BP 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.

There can be no dispute about the benefit of blood pressure lowering. 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 per cent, strokes by 30 per cent, cardiovascular deaths by 18 per cent, and total deaths by 13 per cent, with the benefit being greatest in patients older than 70 years.

However, 'treatment' is more than merely prescribing drugs. The 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.

Combination drug treatment: the 'flexipill'

'Polypills' have been available for many years in different guises. The first 'polypill' was introduced in 1967 for the Veterns Administration Study; SER-AP-ES was a combination of reserpine, apresoline and a thiazide diuretic. This was followed by combination pills composed of thiazide diuretics with potassium or with potassium sparing diuretics, and then by combination pills of beta-blockers with thiazide diuretics and more lately by ACE inhibitors and ACE receptor blockers combined with thiazide diuretics.

These early polypills had the major disadvantage of being fixed-dose combinations. The pharmaceutical industry has now recognised the need for flexible dose combinations within one tablet and I will use the term 'flexipill' to distinguish this therapeutic advance from its much more limited predecessor the 'polypill'.

The 'flexipill' allows a prescribing physician to increase the dosage of the component parts in a single tablet according to blood pressure response. It may be anticipated that further 'flexipill' combinations containing three blood-pressure-lowering drugs will be introduced in future.

The 'flexipill' allows prescribing of low doses of two drugs in one tablet, thereby minimising the adverse effects that might occur with higher doses of the individual components. This advantage provides a means of overcoming therapeutic inertia and improving patient compliance to treatment by avoiding the occurrence of adverse effects and reducing the daily tablet intake.

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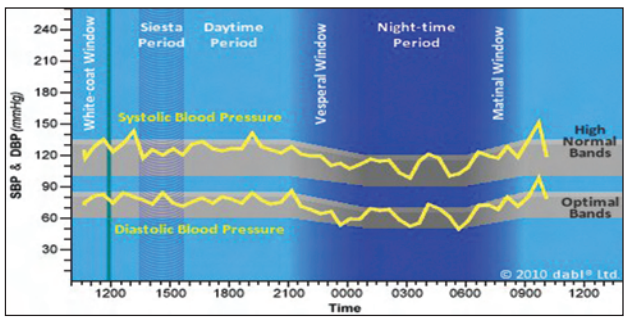

Fig 1: Windows of ambulatory blood pressure

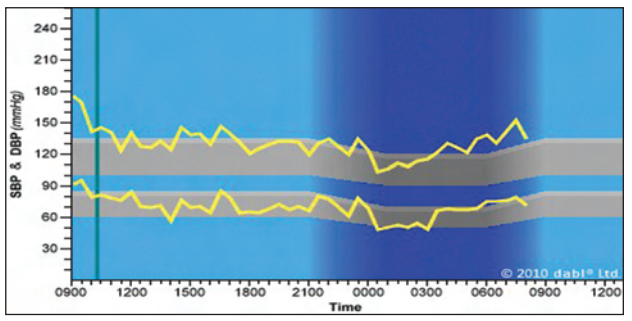

Fig 2: White-coat hypertension (175mmHg/95mmHg) with otherwise normal 24-hour systolic blood pressure (133mmHg daytime, 119 mmHg night-time) and optimal 24-hour diastolic blood pressure (71 mmHg daytime, 59 mmHg night-time). Normal dipping pattern

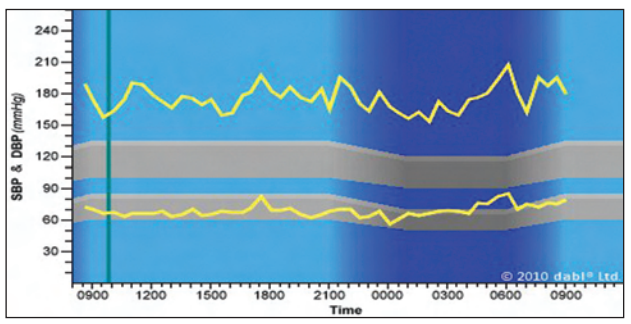

Fig 3: Severe daytime isolated systolic hypertension (176 mmHg/68 mmHg), severe night-time systolic hypertension (169mmHg) and borderline night-time masked diastolic hypertension (70 mmHg)

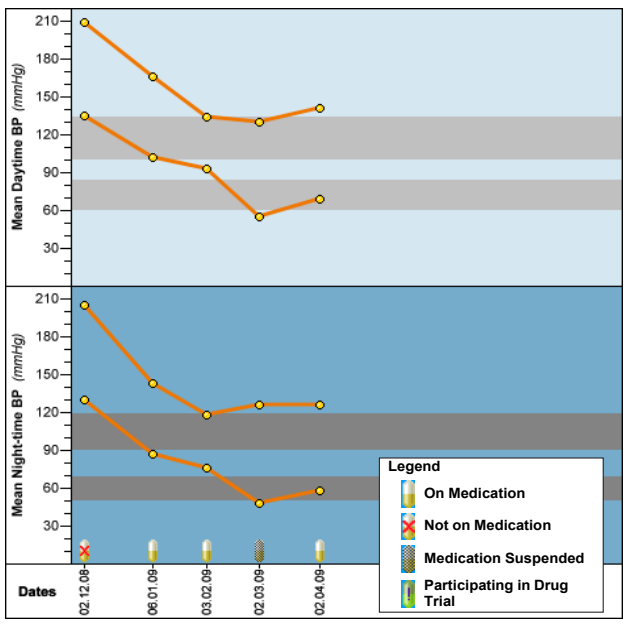

Fig 4: dabl Trend plot for ABPM – daytime blood pressures above, nighttime blood pressures below [generated by dabl ABPM—© dabl 2010]

The following 'flexipills' are available on the Irish market:

ACE INHIBITOR FLEXIPILLS

Acerycal: Perindopril 5 mg/Amlodipine 5 & 10 mg; Perindopril 10 mg/Amlodipine 5 & 10 mg

Capozide: Captopril 12.5 mg/HCTZ 12.5 mg; Captopril 25 mg/HCTZ 25 mg. Captor-HCT: Captopril 25 mg/HCTZ 12.5 mg; Captopril 50 mg/HCTZ 25 mg.

Coversyl Plus: Perindopril 5 mg/Indapamide 1.25 mg; Perindopril 10 mg/Indapamide 2.5 mg.

Lispril-HCTZ: Lisinopril 10 mg/HCTZ 12.5 mg; Lisinopril 20 mg/HCTZ 12.5 mg

Triapin: Ramipril 2.5 mg/Felodipine 2.5 mg; Ramipril 5 mg/Felodipine 5 mg.

Zestoretic: Lisinopril 10 mg/HCTZ 12.5 mg; Lisinopril 20 mg/HCTZ 12.5 mg.

ARB FLEXIPILLS

Benetor Plus: Olmesartan 20 mg/HCTZ 12.5 and 25 mg

Blopress Plus: Candesartan 8 mg/HCTZ 12.5 mg; Candesartan 16 mg/HCTZ 12.5; Candesartan 32 mg/HCTZ 12.5 & 25 mg.

Co-Diovan: Valsartan 80mg/HCTZ 12.5mg; Valsartan 160mg/HCTZ 12.5/25mg; Valsartan 320 mg/HCTZ 12.5 & 25mg.

Coaproval: Irbesartan 150 mg/HCTZ 12.5mg; Irbesartan 300mg/HCTZ 25mg.

Cozaar Comp: Losartan 50 mg/HCTZ 12.5 mg; Losartan 100 mg/HCTZ 12.5 & 25 mg.

Exforge: Valsartan 80mg/Amlodipine 5mg; Valsartan 160mg/Amlodipine 5 & 10mg.

Konverge: Olmesartan 20mg/Amlodipine 5mg; Olmesartan 40mg/Amlodipine 5 & 10mg

Micardis Plus: Telmesartan 40mg/HCTZ 12.5mg; Telmesartan 80mg/HCTZ 12.5 & 25mg.

Omesar Plus: Olmesartan 20mg/HCTZ 12.5 and 25mg

BETA-BLOCKER FLEXIPILLS

Atecor CT: Atenolol 50mg Chlorthalidone 12.5 mg; Atenolol 100mg/Chlorthalidone 25mg

Atenetic: Atenolol 50mg/Chlorthalidone 125 mg; Atenolol 100mg/Chlorthalidone 25mg

Nebilet Plus: Nebivolol 5mg/HCTZ 12.5 and 25mg

RENIN-INHIBITOR FLEXIPILLS

Rasilex HCT: Akiskiren 150mg/HCTZ 12.5 & 25mg; Akiskiren 300mg/HCTZ 12.5 & 25 mg