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Ambulatory Blood Pressure Monitoring in the Diagnosis and Treatment of Hypertension

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Abstract

Clinicians should take initiatives to establish ambulatory blood pressure monitoring (ABPM) services in their own practice, or to ensure that they have access to such services elsewhere. Whenever possible, ABPM should be performed in suitable cases, where it is likely to deliver clinically useful information for making a correct diagnosis, or for tailoring the anti-hypertensive treatment regimen for each individual patient. ABPM is clinically useful, among others, for identifying people with "masked normotension", "masked hypertension", "sleep-time hypertension", and "reduced decline of sleep-time blood pressure". This review briefly outlines the rationales for the use of ABPM, interpretations of the ABPM-derived parameters, and the advantages of ABPM in decision making in the management of hypertension.

Keywords

White-coat hypertension • White-coat effect • Isolated office hypertension • Hypertension in pregnancy • Obstructive sleep apnea syndrome • Resistant hypertension • Non-dipper • Dipping pattern • Normal values for blood pressure

1 Introduction

A fundamental property of blood pressure (BP) is its variability, which is essential for adaptation to numerous changes in the prevailing circumstances. Thus, blood pressures measured at the doctors' offices or clinics are the results of the adaptive responses to, for example, the anxieties and expectations of the patients in those special situations and environments.

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These BPs do not represent the BPs measured outside the clinic at various time points during the days and the nights. In this respect, ambulatory blood pressure monitoring (ABPM) over a 24-h or 48-h period provides more representative information than BP measurements in the office. However, ABPM is expensive, technically more difficult, not available in many of the developing countries, and not widely available even in many centers in the developed countries.

If available, clinicians should use ABPM generously for the diagnosis of, and the follow up of the treatment of hypertension (O'Brien 2016). The technique should be made available more widely both in the primary care centers as well as in the hospital clinics. If the ABPM services do not exist, then the clinicians should take initiatives, and influence the decision makers to make the technique available to the patients at affordable costs.

In this review, I shall address some selected issues for a better understanding of the rationale, and the utility of ABPM, in an attempt to persuade clinicians to use the technique more liberally in their practices. I shall also touch upon some practical issues, which may help clinicians feel comfortable in using the technique, interpreting the results, and making treatment decisions more correctly. For more comprehensive information on ABPM, clinicians may read some recent reviews and guidelines (O'Brien et al. 2013; Parati et al. 2014; Hermida et al. 2013a).

2 When Should Clinicians Use ABPM?

Even when freely available, use of ABPM for all patients will not be cost effective. Physicians need to make decisions about the use of ABPM in individual cases based on sound clinical judgment and experience, even in the absence of convincing evidence, or clear guidelines. In principle, it should be used to identify eventual discrepancies between the office blood pressure measurement (OBPM) and the ABPM. ABPM should be performed, in selected cases, preferably for two consecutive 24 h periods, for confirming the diagnosis of different forms of hypertension, for evaluating the severity of the condition during a 24-h period, for diagnosing sleep-time hypertension, for identifying the dipping patterns, episodes of hypertension or hypotension, and for identifying the patients with autonomic failures (O'Brien et al. 2013). In the following paragraphs, I shall briefly describe some of these conditions.

1. "Masked normotension" (more often called "isolated office-hypertension" or "white-coat hypertension"):

Some patients, who are not on any antihypertensive medicines, have high blood pressure (BP) on repeated measurements (usually day time awake BP) at the doctors' office (OBPM). If ABPM is not available, most doctors will label these patients as hypertensive patients, and they will do so rightly in about 80 % of the cases. However, they will be wrong in about 20 % of the cases, who actually have normal BP (as evidenced from ABPM), but are wrongly diagnosed as hypertensive patients and treated unnecessarily by antihypertensive medicines, often for the rest of their lives. This is a serious problem for the patients and is expensive for the society, and it must be avoided.

Men who have high office BP (>140/90) but whose mean 24-h BP is normal (i.e. ≤130/80 mmHg), do not have hypertension, and should not be treated with antihypertensive drugs (O'Brien et al. 2013). These people have "masked normotension" (also called "white-coat hypertension", or "isolated office- hypertension"), and identification of these people by ABPM is important. They cannot be identified by home blood pressure monitoring (HBPM), which cannot measure sleep-time BP, an important marker of cardiovascular disease (CVD) risk. These people should be followed up by ABPM within two years, if they do not have an increased risk for CVD (e.g. diabetes, chronic kidney disease, or past CVD), or within one year, if they have an increased CVD risk.

In the USA, the Centers for Medicare and Medicaid Services approves reimbursement for the use of ABPM for identification of people with "masked normotension". Early use of ABPM for the diagnosis of "masked normotension" is recommended, among others, by the Canadian Hypertension Education Program (CHEF), UK National Institute for Health and Clinical Excellence (NICE), the European Society of Hypertension, and the International Society for Chronobiology (O'Brien et al. 2013; Hermida et al. 2013a; Gelfer et al. 2015; Krause et al. 2011). U.S. Preventive Services Task Force (USPSTF) concludes that ABPM is the reference standard for confirming elevated office BP results to avoid misdiagnosis and overtreatment of persons with isolated office-hypertension (Piper et al. 2015). ABPM before starting treatment of hypertension is cost-effective (Lovibond et al. 2011).

It should be noted that if office BP is $\geq$180/110, doctors need to start treatment without waiting for ABPM. First-time ABPM should not be done for patients who are on $\leq$2 antihypertensive medicines. If they are on $\geq$3 antihypertensive medicines then they should be tested by ABPM to confirm if they have true resistant hypertension (see below).

2. "Masked hypertension":

Many people, who are not on any antihypertensive medicines, have normal office BP measured on repeated occasions. It is important for clinicians to keep in mind that about 10 % of these people may have hypertension, despite normal office BP ("masked hypertension"). In some cases "masked hypertension" is due to sleep-time hypertension. "Masked hypertension" is common and is associated with increased risk for CVD events (Hermida et al. 2012; Booth et al. 2016). If the diagnosis of hypertension is missed in people with "masked hypertension", they will remain untreated with increased risk for CVD. For the diagnosis of "masked hypertension", clinicians should use ABPM whenever they suspect the condition.

3. "Sleep-time hypertension" and "dipping" or "rising" patterns of BP:

Sleep-time hypertension and the "dipping" or "rising" patterns of BP during sleep-time can be identified only by using 24-h ABPM (preferably on two consecutive days). It should be noted that for defining the wake-time BP and the sleep time BP, it is common and convenient to use arbitrary fixed clock hours, for example, wake-time BP defined as BP measured during 09:00–21:00, and sleep-time BP defined as those during 01:00–06:00. However, presentation of ABPM results in terms of clock hours can be misleading. For accurately measuring the average wake-time and sleep-time BPs, people undergoing ABPM must note down in a diary the times of retiring to the bed at night, and the times of awakening in the morning, and the ABPM results must be presented in terms of "hours from bedtime" (Hermida et al. 2013a).

Some people have normal office BP, and normal ABPM-derived mean wake-time BP, but high ABPM-derived mean sleep-time BP. The latter is an independent, and a better predictor of CVD morbidity and mortality compared to the office BP or ABPM-derived mean wake-time BP, or mean 24 h BP (Hermida et al. 2016). Sleep-time relative systolic BP (SBP) decline has additional prognostic value. Sleep time relative SBP decline or "dipping" is calculated as 100$\times$ (mean wake-time SBP $-$ mean sleep-time SBP)/mean wake-time SBP. Sleep-time relative SBP decline is a continuous variable but it is conventional to divide people into four groups based on the decline: people who have $>$10 % decline in sleep-time SBP compared to the wake-time SBP are called "dippers"; those who have $<$10 % decline are called "non-dippers"; those who have $>$20 % decline are called "extreme dippers"; and those who have $<$0 % decline are called "risers". It should be noted that in shift-workers, the circadian rhythm of BP is reversed. They have peak BP at about 10:00–11:00 (Sternberg et al. 1995).

The frequency of sleep-time hypertension, "non-dipping", "reduced-dipping" or "riser"

patterns of BP is high (as high as 65–81 %) in the elderly people, type 2 diabetes, chronic kidney disease, obstructive sleep apnea and other sleep disorders, resistant hypertension, obesity and pregnancy (Hermida et al. 2016; Mojon et al. 2013; Ayala et al. 2013). Moreover, about 20 % "normotensive" people are "non-dippers", and thus have increased CVD risk. ABPM should be performed when sleep-time hypertension, "reduced dipping", "non-dipping" or "rising" patterns of sleep-time BP are suspected. Identification of sleep-time hypertension and the "non-dippers" is clinically useful, since some of these patients can be treated by administering some of the antihypertensive medicines, in full dose, at the bed-time (not traditional BID regimen) (Hermida et al. 2016).

4. Resistant hypertension:

Hypertension that is not controlled by lifestyle changes and therapeutic doses of $\geq$3 antihypertensive medicines (including a diuretic, unless contraindicated) is called resistant hypertension. Thus, all patients who need $\geq$4 medicines for control of BP have resistant hypertension. Diagnosis of resistant hypertension based on OBPM can often be wrong because of the well-known "white-coat effect". In one large study, 37.5 % of the "resistant hypertension" patients diagnosed by OBPM had "white-coat resistant hypertension", and 62.5 % had true resistant hypertension, as verified by ABPM (de la Sierra et al. 2011). ABPM is essential for a correct diagnosis of resistant hypertension (Lazaridis et al. 2015). It is also useful for guiding the treatment of hypertension in these patients. When any treatment of these patients is modified in any way, the results of such modifications should be evaluated by repeating ABPM within the ensuing three months.

5. Evaluation of the treatment of hypertension:

ABPM is useful for choosing the optimal treatment regimen for any individual hypertensive patient, and to monitor if the treatment has resulted in the desired BP goals. Follow up of patients by repeated ABPM can allow changes of treatments, reduction of multidrug treatment or even total withdrawal of anti-hypertensive medicines and improved BP control (Grin et al. 1993; Staessen et al. 1997).

Some patients who are on the treatment by antihypertensive medicines have high BP measured at the office, but have normal or lower BP measured by ABPM. Some patients have normal wake-time BP, but high sleep-time BP. Some patients have reduced decline of sleep-time BP. Some patients develop symptoms suggestive of hypotension during the treatment with anti-hypertensive medicines. Ideally, antihypertensive medicines should reduce BP in a homogeneous and smooth manner throughout the day and the night. In reality, many long-acting BP-lowering medicines do not reduce BP homogeneously over an entire 24-h period. Thus, long-acting BP-lowering medicines taken once only in the morning may not reduce sleep-time BP or may not induce adequate decline of the sleep-time BP. If some BP lowering medicines are taken at the bed-time, it can reduce the sleep-time hypertension, and restore the normal dipping pattern in some patients (Hermida et al. 2013b).

6. ABPM in pregnancy

For ABPM in pregnancy, doctors should use only those ABPM devices that have been validated for use in pregnancy. ABPM is clinically useful in early pregnancy to distinguish the women who have true hypertension from those who have "masked normotension" or "white-coat hypertension". In one study about 50 % of the women, who were diagnosed for the first time by OBPM to have hypertension, had actually "masked normotension" or "white-coat hypertension" as confirmed by ABPM (Brown et al. 2005). There is no conclusive evidence that ABPM can predict pre-eclampsia. In gestational hypertension and pre-eclampsia, the frequency of sleep-time hypertension is high, but these patients also have wake-time hypertension (Brown et al. 2001).

Normally, BP in pregnant women is lower than that in non-pregnant women. In normal pregnancy BP successively decreases up to the middle of pregnancy and then successively increases up to the delivery. BP ranges and the upper normal values for 24 h BP and sleep-time BP (defined as mean + 2 standard deviation), in different weeks of pregnancy have been reported by several groups and one such set of values are given below (O'Brien et al. 2013; Higgins 2001):

9–17 weeks: 24 h BP: 101/60-118/71. Upper normal value for 24 h BP: 121/73. Sleep-time BP: 93/50-109/64. Upper normal value for Sleep-time BP: 110/64.

18–22 weeks: 24 h BP: 96/56-127/78. Upper normal value for 24 h BP: 126/76. Sleep-time BP: 88/46-120/68. Upper normal value for sleep-time BP: 114/66.

26–30 weeks: 24 h BP: 97/56-133/84. Upper normal value for 24 h BP: 128/78. Sleep-time BP: 87/46-125/76. Upper normal value of Sleep-time BP: 117/68.

31–40 weeks: 24 h BP: 103/57-136/85. Upper normal value for 24 h BP: 131/82. Sleep-time BP: 85/46-131/77. Upper normal value for sleep-time BP: 123/72.

ABPM is also useful than OBPM for diagnosing sustained hypertension during late post-partum period in women who had gestational hypertension or pre-eclampsia during pregnancy (Mangos et al. 2012).

3 Reference Values for ABPM

Reference values for ambulatory BPs are lower than those for office BP. Based on the CVD outcome, the following diagnostic threshold values have been recommended for ambulatory BPs (Hermida et al. 2013a). For adult men, mean wake-time BP: 135/85 mmHg, and mean sleep-time BP: 120/70 mmHg (Kikuya et al. 2007). For adult women, mean wake-time BP: 125/80 mmHg, mean sleep-time BP: 110/65 mmHg (Hermida et al. 2013c). For high risk patients (e.g. those with diabetes, chronic kidney disease, previous CVD events) of both sexes, mean wake-time BP: 120/75 mmHg, and mean sleep-time BP: 105/60 mmHg (Hermida et al. 2013a).

4 Performing ABPM and Interpreting the Results

Doctors working in the primary care centers or in hospital clinics should take initiatives to establish their own ABPM services, if those do not already exist. Price of ABPM device with software in 2016 is around 2500 USD. Alternatively, doctors should know where to refer their patients to for ABPM. Doctors and nurses responsible for ABPM services and analysis of the results must receive appropriate training, and keep themselves updated.

Many automated ABPM devices that measure blood pressure by oscillometric method are available. These devices do not measure the SBP and the DBP directly; rather they measure the mean arterial BP and then deduce the SBP and DBP from the oscillometric pressure changes by using algorithms that are often kept secret and are specific to the respective devices. For this reason, it is important to use devices that have been independently validated by internationally accepted protocols, for their accuracy, for use in different patient groups (e.g. in the elderly, in pregnancy). For a list of recommended ABPM devices check this website: http://www.dableducational.org/sphygmomanometers/devices_3_abpm.html. The devices should be recalibrated yearly by companies that meet the ISO 9001 standards. The batteries should be checked regularly. The software must be able to generate a standardized report, including the raw BP and heart-rate data, blood pressure plots, software generated mean wake-time and sleep-time BP, and sleep-time BP decline (dipping in %) (Omboni et al. 2015).

At the outset, it is necessary to assess whether the patient is able to understand and follow the instructions, and cooperate during the ABPM process. Patients must receive a number of clear verbal and written instructions. On the day of the monitoring, they will carry on

their normal activities as much as possible, but they must avoid physical exercise and activities that may interfere with the recording of representative BP values (e.g. driving and day-time sleeping). The ABPM devices give a beep sound a few seconds before starting the inflation of the cuff. At the time of the inflation, the person will stand still or sit down, without talking, with the arm relaxed at the heart level. At night, the beep sound must be shut off, but the monitor must stay on, and it can be placed on the patient´s side. If the device is removed for short periods, for example, for a shower, it should be switched off. They must maintain a diary where they note down the times of retirement to the bed at night, waking in the morning, meals, taking medicines, and other events. They must know how to switch off the device, when needed, and exactly when and where they should return the device.

Measure the arm circumference, and BP in both arms, and apply a blood pressure cuff of appropriate size to the dominant arm. If there is $>$10 mmHg difference in BP between the arms then use the arm with higher BP for ABPM. The patient should not be able to see the BP values displayed on the device during the monitoring. Program the ABPM device to measure BP at 15–60 min intervals (often at 20–30 min intervals during the wake-time, and at 60 min interval during the sleep-time). It should be noted that, the reproducibility of the BP patterns depends more on the duration of monitoring (preferably for 24 h on two consecutive days) than on the sampling rate (Hermida et al. 2013d).

At the time of interpreting the ABPM results, it is first of all essential to check if the monitoring has been done satisfactorily (Omboni et al. 2015). If ABPM records $\geq$70 % of the scheduled measurements, $\geq$20 valid measurements during the wake-time and $\geq$7 measurements during the sleep-time, than it can be accepted as a satisfactory monitoring (Parati et al. 2014). The monitoring cannot be accepted as entirely satisfactory if data are lacking for more than two, consecutive hourly intervals, if the patient sleeps during the night for less than 6 h or more than 12 h, or if the measurements were done during exercise, driving, excessive movement, or during unusual emotional stress (Hermida et al. 2013a). Look at the BP traces for episodes of high or low BPs. A report of analysis of the ABPM should include the dates of the performance of the monitoring, comments on the quality of the recording, mean 24 h BP, mean wake-time BP, mean sleep-time BP, and degree of "dipping" in percent.

5 Difficulties of ABPM

The main problem with ABPM is that it is either not widely available or not used by doctors even when it is readily available. OBPM is faster, cheaper and more convenient to most doctors. Some patients may find ABPM inconvenient especially during the sleep-time and especially if ABPM has to be done repeatedly. Some people do not tolerate ABPM at all and others fail to follow the instructions despite clear instructions, making good quality monitoring difficult. It may be difficult to perform ABPM in some very obese people and results can be wrong if cuffs of appropriate size are not used. In atrial fibrillation ABPM is less accurate in measuring the diastolic BP but ABPM is not contraindicated in this condition.

6 Concluding Remarks

Numerous researches over past three decades have established ABPM as an evidence-based and cost-effective gold-standard for the diagnosis and treatment of hypertension. Use of ABPM can reduce misdiagnosis, and unnecessary treatment, and lead to better control of BP. Clinicians should use ABPM whenever possible and take initiatives to establish ABPM services where those do not exist.

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Conflict of Interest None

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