Second international consensus meeting on twenty-four-hour ambulatory blood pressure measurement: consensus and conclusions

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Introduction

Non-invasive ambulatory blood pressure monitoring was first developed 30 years ago, and is now evolving from its former role as a somewhat esoteric research tool to becoming a clinically useful procedure for the evaluation of hypertensive patients. The developing interest in ambulatory blood pressure monitoring in clinical medicine has been reflected in a huge outpouring of publications on the application of the technique. This consensus report reviews the present state of the art as presented at the Dublin Consensus Meeting held in the Royal College of Surgeons in September 1991, and discusses some of the outstanding scientific and clinical issues.

Methodology

At least 15 different brands of monitor are now commercially available, virtually all of which take intermittent measurements from a cuff over the brachial artery. In the past few years there have been considerable advances in the technology of ambulatory blood pressure monitors, resulting in smaller, quieter devices which are more accurate and cause minimal inconvenience. Gratifying though these developments have been, a number of problems remain.

The present generation of ambulatory monitors can supply a reasonably accurate estimate of the average level of blood pressure but, for two reasons, they provide an inadequate estimate of blood pressure variability. First, they are very sensitive to movement artefacts, which means that they cannot accurately record blood pressure occurring during physical activity [1]. Secondly, they sample only a small proportion of the total number of blood pressure values [2]. The development of the Portapres, a device capable of measuring continuous 24-h blood pressure non-invasively from the finger, is a prospect which could permit beat-to-beat analysis of the 24-h blood pressure profile [2,3]. Twenty-four-hour ambulatory blood pressure monitoring began with the technique of direct intra-arterial measurement, which has provided much valuable information on blood pressure behaviour and has stimulated the development of non-invasive techniques. However, because of its invasive nature, the technique is not used in the routine clinical evaluation of hypertension [4]. Direct measurement has, however, been used to evaluate the ambulatory performance of ambulatory blood pressure monitors [2].

New systems for ambulatory blood pressure monitoring must be validated independently by a reputable laboratory, ideally both in the laboratory and under field conditions [1,2,5]. Eight ambulatory systems have now been validated according to the British Hypertension Society protocol. With a standardized validation protocol, it is possible to compare the accuracy and performance features of different systems [5]. In the United States the Association for the Advancement of Medical Instrumentation (AAMI) is revising its national standard (personal communication from AAMI, 1991). An issue that has not been standardized so far is the extent to which different ambulatory blood pressure monitors are subject to movement artefacts, a feature that may vary between models, and to the effects of posture [1,2,5].

Ambulatory activity monitoring has great potential as a research procedure when combined with blood pressure monitoring, because it has been demonstrated that changes in activity account for a major propor-
Introduction

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Despite the underpinning that science provides for the practice of medicine, there is a surprising diversity in the diagnosis and management of common conditions in various countries. This is well exemplified in hypertension, where the pattern of drug use differs quite markedly from country to country, even within Western Europe. Therefore, it should come as no surprise when we consider rapidly developing areas of research and clinical practice, in this case ambulatory blood pressure measurement, that there should also be a variety of approaches and views, ranging from black nihilism to unquestioning acceptance. It is not only desirable, therefore, but essential that scientists meet to review the current state of knowledge of the technique and to attempt to reach a consensus on the use of ambulatory blood pressure measurement in the diagnosis, prognosis and management of raised blood pressure.

Wolfgang Meyer-Sabellek initiated the process by holding the first Consensus Meeting on Ambulatory Blood Pressure Measurement last year, but given the rapidly expanding literature on the subject, we considered it timely to organize a second meeting in Dublin in September this year. We were pleased that so many of the world leaders in the field were able to join us for what was a most exciting academic occasion. The Meeting was enhanced by being held in conjunction with the British Hypertension Society Annual Scientific Meeting, and we thank the Society for recognizing us in this way. We are also pleased to acknowledge the help of ICI Pharma in providing us with an educational grant to make the venture financially feasible and the Charitable Infirmary Charitable Trust which has supported research on ambulatory blood pressure in the Blood Pressure Unit at Beaumont Hospital.

The Meeting had a further piquancy for us in that the venue for the meeting, the Royal College of Surgeons in Ireland Medical School, is a uniquely cosmopolitan one, with students from more than 30 countries. Thus, we are well used to international interaction. While our students have an identity of purpose in the medical school here, we do not attempt to develop consensus; rather, we revel in the variety and richness of outlook and value the views of the individual. The Consensus Meeting had much of this flavour, but of course, we were obliged to find common ground to provide a document that would be seen to represent the state of the art as of September 1991. Clearly this consensus is not final, but by virtue of the rapid developments in ambulatory blood pressure measurement, can only be provisional. We await the results of many definitive studies, not least those linking ambulatory blood pressure measurement data with hard endpoints in hypertension. Accordingly, Professor Tom Pickering has agreed to hold the third Consensus Meeting in the United States next autumn. With appetites whetted in both Berlin and Dublin, we look forward to his meeting with keen anticipation.
tion of changes in 24-h blood pressure. Moreover, the technique provides an easily quantifiable measure of activity and may also give an objective measure of sleep [6].

Data analysis

There is still disagreement over the best method of analysing ambulatory blood pressure data, but the different techniques are appropriate for different purposes and therefore it is unlikely that any single technique will satisfy all requirements. The ideal techniques should be statistically valid, physiologically meaningful and clinically useful [7]. The general requirements are that analytical methods should provide measures of the average level of blood pressure over the 24-h period, during the day and during the night, and the pattern of change over 24 h. The origins of the diurnal rhythm of blood pressure are still controversial, with two competing theories, which may be called the 'set point' and 'oscillator' models [9]. The former assumes that there are two tonic levels of blood pressure corresponding to wakefulness and sleep, about which phasic changes occur, the major determinants of blood pressure being activity and arousal. The oscillator model assumes that there is an intrinsic circadian rhythm, which is determined more by the time of day than by arousal and activity. Most of the evidence favours the set point model, and analysis of the diurnal rhythm according to the oscillator mode, using either the cosinor method or Fourier analysis, has to incorporate harmonics to allow for the fact that the typical blood pressure rhythm does not consist of peaks and troughs 12 h apart. It is important to note that the Fourier method for the parametrization of the diurnal blood pressure profile is nothing more than a statistical technique describing the level of blood pressure as a function of time throughout the day.

Dippers and non-dippers

One of the more intriguing findings with ambulatory blood pressure monitoring has been the recognition that the usual nocturnal fall in blood pressure is diminished or absent in some subjects. This occurs both in normotensives (particularly among blacks in the United States [10]) and in hypertensives, and has led to adoption of the terms 'dippers' (for the normal pattern) and 'non-dippers'. Non-dippers are seen in several types of secondary hypertension (e.g. Cushing's syndrome, phaeochromocytoma and pre-eclampsia) and in some cases of essential hypertension [11]. The mechanisms remain unexplained. The first question is whether the phenomenon represents some ab-

normality of sleep itself or is primarily a disorder of blood pressure regulation. The exact definition of the phenomenon is also not fully agreed upon, but is usually some measure of the difference between daytime and night-time blood pressures. However, this difference will depend not only on how far the pressure falls at night, but also on how far it rises during the day [9,10]. Thus, differences in daytime activities could also be responsible for whether a subject is characterized as a diper or non-dipper. As the nocturnal fall in blood pressure appears to be normally and continuously distributed, the distinction between dippers and non-dippers is arbitrary. It is tempting to suppose that the non-dipping pattern may be a risk factor for cardiovascular disease, and there is some evidence that non-dippers have a greater left ventricular mass than dippers [12]. This topic needs, and is likely to receive, further attention.

Antihypertensive treatment

Ambulatory monitoring is a valuable technique for evaluating antihypertensive drug efficacy in clinical practice as well as in research [13]. Ambulatory blood pressure monitoring can demonstrate both the efficacy and the duration of the drug effect, and also the nocturnal effects of antihypertensive drugs [14]. The relative lack of a placebo effect and the increased reliability of ambulatory monitoring compared with conventional measurement, which are consequences of the larger number of measurements obtained with ambulatory blood pressure monitoring, permits reduction of the sample size needed to detect a given effect and may render placebo control unnecessary [15]. Ambulatory monitoring provides an interesting opportunity to study the effects of antihypertensive medication on the diurnal rhythms of blood pressure. This may be of theoretical relevance in understanding the physiological mechanisms of blood pressure regulation, as well as being of clinical relevance in selecting the most appropriate antihypertensive drug [13].

In most published studies of antihypertensive drug efficacy, patients were selected for inclusion on the basis of clinic blood pressures, resulting in the inclusion of many patients with white-coat hypertension. With ambulatory blood pressure monitoring, these patients may be identified and excluded from entry [15].

In spite of the many advantages of ambulatory blood pressure monitoring in evaluating antihypertensive drugs, the technique is not a requirement for approval of a drug by governmental regulating agencies in the United States or Europe [16,17]. Although the United States Food and Drugs Administration does not demand ambulatory blood pressure monitoring at present, it does accept 24-h data if available and encourages measurement of blood pressure on more
than one occasion during a dosing interval [16]. The
day cannot be far off when ambulatory blood pres-
sure monitoring will become a mandatory requirement
for new drug applications in the European Community
[17].

Definition of 'normal' 24-h ambulatory
pressures

Considerable effort is being expended to define the
range of ambulatory blood pressure in normal sub-
jects [18–29]. Three approaches, each based solely
on blood pressure, are currently being used. The first
takes the 95th centile (or 2 standard deviations) as the
upper limit of blood pressure for a normal population.
The problem here is that the 95th centile of a truly
population-based sample is likely to be much higher
than any acceptable cutoff point, because the preva-
ience of hypertension in the population is more than
5%. Therefore, it is necessary to exclude the 'hyper-
tensives'. This, however, has to be done on the basis
of clinic blood pressures, so the definition of normal
values will be largely determined by the criteria used
for defining hypertension, and this limits the validity
of the method.

A second method is to establish the level of ambu-
latory blood pressure that is equivalent to a particu-
lar clinic blood pressure level, such as 140/90 mmHg
[22]. The regression line relating clinic and ambulatory
blood pressures for a population of normotensives
and hypertensives can be used to define this, but the
procedure is difficult; although the mean ambulatory
blood pressure corresponding to a given clinic pres-
sure can be easily predicted, the error in predicting
the ambulatory blood pressure in individual patients
is much too large for clinical purposes. This method
has the advantage of being independent of any prior
definition of hypertension in selecting the reference
population, but is still based on an arbitrary reference
point, the clinic pressure.

A third method uses the concept of blood pressure
load, which is defined as the percentage of readings
above a certain level [30]. This approach is faced with
the same selection problems as in the first method and
is even more unsatisfactory, as it depends on an arbi-
trary threshold level.

An alternative approach to the three methods de-
scribed is to relate blood pressure to cardiovascular
risk, either directly as cardiovascular morbidity, or in-
directly by relating blood pressure to an index of tar-
get organ damage, such as left ventricular hypertrophy
[31]. In either case, the relationship between blood
pressure and risk is likely to be steeper for ambulatory
than for clinic blood pressure. Although theoretically
preferable to methods that rely solely on blood pres-
sure, these methods are much more expensive to carry
out and it will be many years before data are avail-
able. A further drawback is the fact that the relation-
ship between ambulatory blood pressure and the inci-
dence of cardiovascular complications is continuous.
Indeed, there is no threshold above which the risk sud-
denly increases, and the decision about what level of
risk is acceptable must be an arbitrary one. Neverth-
less, such methods provide the only way of determin-
ing those levels of ambulatory blood pressure that are
truly healthy, and at least two longitudinal studies are
now underway [32–34].

While awaiting the outcome of these studies, and given
the rapid application of ambulatory blood pressure
monitoring in clinical practice, it is important to have
a working definition of normal values which will be
dependent on data derived from studies of clinically
determined normotensive populations. There are now
a large number of these studies in different popula-
tions [18–29] and it is hoped that a meta-analysis
may provide the information required for defining more
precise age- and sex-specific diagnostic criteria. Thus,
guidelines may be obtained for the application of nor-
mal values in the clinical use of ambulatory blood pres-
sure monitoring [35].

Clinical application

The most important clinical application of ambulatory
blood pressure monitoring is the evaluation of patients
with borderline hypertension, in whom the decision to
start treatment rests on an accurate assessment of true
blood pressure [13]. If it is accepted that patients with
normal ambulatory blood pressures but raised clinic
blood pressure (white-coat hypertension) do not need
treatment, there is a prospect that ambulatory mon-
itoring could be very cost-effective [36]. It has been
estimated, for example, that the number of patients
with mild hypertension needing antihypertensive treat-
ment can be reduced by nearly 75% without increasing
morbidity [36]. Ambulatory blood pressure moni-
toring may also be particularly helpful in selecting the
most appropriate drug and dosing interval for an indi-
vidual patient and in assessing the response to treat-
ment [13].

In patients with secondary hypertension the procedure
is of limited value, because the altered diurnal pattern
is non-specific. However, the loss of the normal no-
turnal dipping pattern may alert the clinician to look

Ambulatory blood pressure monitoring also plays a
role in assessing patients with symptoms suggestive of
postural or drug-induced hypotension [13,37].

A major question awaiting attention is the recognition
of the procedure by reimbursing agencies. In most
countries ambulatory blood pressure monitoring is
not approved for routine clinical use, but this situation is changing rapidly. While most experts in the field believe that ambulatory monitoring does have a clinical role, there is also concern that the technique might be used excessively, particularly if the physician has a direct financial incentive to perform the test. The number of patients with questionable blood pressure elevations is so enormous that it is important to lay down guidelines for the application of ambulatory blood pressure monitoring in clinical practice [13].

Special groups

Ambulatory blood pressure monitoring may be particularly useful in determining the presence of hypertension in children and adolescents, where the accuracy of diagnosis is of great importance, and in the elderly, in whom excessive treatment is particularly to be avoided [38]. Special considerations have also to be given to the interpretation of 24-h blood pressure profiles in blacks [10].

It might be anticipated that ambulatory monitoring would be of value in the diagnosis of pregnancy-induced hypertension, a condition in which measurement of blood pressure by conventional methods is unreliable. Indeed, it is hoped that the technique may allow early identification of women at risk of developing pre-eclampsia, and that this has prompted a number of studies [39–43], which have been summarized in [44].

Prognosis

The most important question now awaiting an answer is how accurate ambulatory blood pressure is in predicting long-term morbidity and mortality. There is evidence that ambulatory blood pressure monitoring is superior to conventional blood pressure measurement in this regard [45], and there is also evidence from target organ endpoints that ambulatory blood pressure monitoring is better correlated with end-organ involvement than clinic blood pressure is [12,31], but the outcome of the longitudinal studies now underway must be awaited before the use of this technique in the prognosis of hypertension can be determined definitively.

Whereas many of the issues discussed at the Dublin meeting eluded consensus for the moment, there was general agreement that ambulatory blood pressure measurement has moved from the research arena to clinical practice, and that it is therefore essential to ensure that guidelines are enacted regularly, reflecting advancing knowledge of the technique.

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