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Ambulatory Blood Pressure Monitoring in Pediatrics

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Abstract

Purpose of Review This is a review of ambulatory blood pressure monitoring (ABPM) use in pediatrics, summarizing current knowledge and uses of ABPM.

Recent Findings Updated guidelines from the American Academy of Pediatrics have emphasized the value of ABPM. ABPM is necessary to diagnose white coat hypertension, masked hypertension, and nocturnal hypertension associated with specific conditions. There is growing evidence that ABPM may be useful in these populations. ABPM has been demonstrated to be more predictive of end-organ damage in pediatric hypertension compared to office blood pressure.

Summary ABPM is an important tool in the diagnosis and management of pediatric hypertension. Routine use of ABPM could potentially prevent early cardiovascular morbidity and mortality in a wide variety of populations.

Keywords Ambulatory blood pressure monitoring · ABPM · Pediatric hypertension · Hypertension in children and adolescents · Pediatric cardiovascular disease

Introduction

Obtaining accurate blood pressure (BP) measurements in children, especially in very young children, can be a challenge. These measurements can vary due to interactions among environmental, behavioral, and neurohormonal factors [1]. Incorrect cuff size is a major contributor to measurement error. Multiple studies have identified a lack of appropriately sized cuffs in both outpatient and inpatient settings [2–5]. Ideally, BP is measured while the patient is seated with their feet flat on the floor, has their arm supported at heart level, and is not speaking; however, this setting can be difficult for a child to comply with. Anxiety can play a role in measurement error as office BP measurements are subject to white coat effect. Outside factors, such as recent caffeine intake, can also affect the BP reading [6].

Oscillometric devices are commonplace due to their ease of use, lack of arm preference, and automation. However, these devices have inherent inaccuracies [7]. Oscillometric devices measure the mean arterial pressure directly and then calculate the systolic and diastolic BP based on software proprietary to the device manufacturer [8]. Consequently, these measurements are subject to considerable variation between different manufacturers.

Yet, regardless of the method used to measure the BP, the office BP only provides a snapshot of a continuously changing physiologic variable. In adults, home BP measurements are frequently utilized to provide additional information regarding this variability. Unfortunately, the lack of validated home devices for use in children and the lack of normative pediatric home BP data limit a similar practice in pediatrics [7]. BP is continuously varying throughout a 24-h period and is normally ~ 10% higher during waking hours than during sleep. BP may vary between visits and even during the same visit [9•]. In a study of adolescent BP, only 56% of subjects had the same BP category on 3 different visits [10]. Due to the variable nature of BP, the diagnosis of pediatric hypertension requires persistence of elevated BP over time, suggesting that a method of measuring continuous BP may be useful in the evaluation of elevated BP.

Ambulatory blood pressure monitoring (ABPM) is well established in the assessment and treatment of hypertension

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in adults. This practice is increasingly being used in pediatrics as ABPM avoids many of the previously discussed drawbacks. ABPM provides a more comprehensive BP assessment as it is based on multiple BP measurements obtained over a 24-h period. In a study evaluating office BP and ABPM, it was found that using the office BP measurement alone misclassified BP status in over 75% of subjects [11]. In addition, use of ABPM in children has been shown to be more predictive of target organ damage, such as left ventricular hypertrophy, increased carotid intima-media thickness (cIMT), and arterial stiffness compared to office BP [12]. The American Academy of Pediatrics Clinical Practice Guideline places emphasis on the use of ABPM in diagnosing and managing hypertension [9•]. The statement recommends placement of an ABPM in any child who has elevated BP for 1 year or more or with stage 1 hypertension over 3 clinic visits, in any child with suspected white coat hypertension, or in any child that is at high risk of developing hypertension. Additional patient populations to consider performing ABPM include children and adolescents with chronic kidney disease, a history of solid organ transplant, a history of aortic coarctation repair, type 1 or 2 diabetes, or obstructive sleep apnea (each of these indications will be discussed in greater detail in this review).

The remainder of this review will briefly discuss ABPM placement and performance. Additionally, a detailed discussion of recent literature describing pediatric ABPM use with attention to specific patient populations to consider its use will follow.

Conducting ABPM

A more comprehensive description was published by the American Heart Association in 2008 with subsequent updates in 2012 and 2014 [7, 12, 13•].

Patient history should be reviewed for contraindications to ABPM placement, including severe clotting disorders, rhythm disturbances, or latex allergy (depending on specific ABPM equipment being used). An ABPM device, consisting of a lightweight monitor and an appropriately sized cuff, is worn in the child's home environment, providing more accurate measurements of their BP, including while asleep. The cuff should be selected based on published guidelines and placed on the non-dominant arm, to allow for daily activities unless the patient has had arterial surgery on that side, for example, coarctation of the aorta repair or creation of an arteriovenous fistula [14]. After application, the ambulatory BP should be measured and compared with resting, clinic BP using a similar technique. If the average of 3 values is greater (or lesser) by 5 mmHg or more, cuff placement should be adjusted or the device checked for calibration. The patient and their parents should receive education regarding the monitor, including details such as the arm should be held still during each measurement and a diary should be completed recording awake and sleep times, as well as other things that could affect blood pressure, such as activity and exercise, pain, stress, and timing of medication administration. Symptoms (e.g., dizziness) should also be recorded. Monitors should be programmed to obtain readings every 15–20 min while awake and every 20–30 min while asleep. At a minimum, 1 valid reading per hour should be obtained with at least 40 readings over the entire 24-h monitoring period for the study to be considered adequate. Children should be encouraged to participate in their routine activities. It has been demonstrated that successful ABPM can be performed in most patients, even while sleeping [15].

For interpretation, the mean systolic BP and diastolic BP are calculated for the 24-h study period as well as daytime and nighttime periods based on diary report. BP load is the proportion of readings above thresholds values, which are generally set at the 95th percentile for gender and height from age- and gender-specific reference ABPM data [16]. BP loads of 25–50% are considered pathological and those above 50% have been demonstrated to be predictive of left ventricular hypertrophy [17]. BP staging is dependent on office BP and mean ambulatory BP and BP load for either systolic or diastolic BP (Table 1). There will be patients who do not fall into any of these categories and should be evaluated individually to determine their BP classification, considering the presence or absence of underlying secondary causes of hypertension or specific cardiovascular risk factors. ABPM is not performed in children < 5 years of age as normative data does not exist for this age group and younger children typically do not tolerate ABPM testing.

Nocturnal Dipping

Nocturnal dipping is defined as 10–20% decrease in mean systolic and diastolic BP from daytime to nighttime periods. Non-dipping status (< 10% decrease) and reverse-dipping status (when the average nighttime BP is greater than the daytime BP) are associated with worse outcomes in adults [18, 19]. Both statuses are frequently observed in chronic kidney disease, type 2 diabetes, and obstructive sleep apnea [20]. Fewer studies evaluating non-dipping and reverse dipping have been performed in pediatric populations. A retrospective study of obese children identified a significant association between non-dipping status and obesity, similar to adults [21•]. Among hypertensive children, patients with a non-dipping status have been found to have a more severe degree of hypertension [22]. Based on these studies, it appears that abnormalities in nocturnal dipping occur parallel in children as has been well established in adults.

Table 1 Staging schema based on pediatric ambulatory blood pressure monitor data

Classification	Office blood pressure	Mean ambulatory blood pressure[§]	BP load (%)
Normotensive	< 90th percentile	< 95th percentile	< 25
White coat HTN	≥ 95th percentile	< 95th percentile	< 25
Prehypertension	≥ 90th percentile or > 120/80 mmHg	< 95th percentile	≥ 25
Masked HTN	< 95th percentile	> 95th percentile	≥ 25
Ambulatory HTN	> 95th percentile	> 95th percentile	25–50
Severe ambulatory HTN	> 95th percentile	> 95th percentile	> 50

HTN, hypertension; SBP, systolic blood pressure; DBP, diastolic blood pressure

[§] For either the wake or sleep period of the study, or both

ABPM with Pediatric Hypertension Outcomes

Adult studies have consistently reported superiority of ABPM parameters over office BP in predicting mortality, cardiovascular events, and target organ damage [23–25]. Comparable pediatric data does not exist due to very low incidence of mortality and cardiovascular events. Alternatively, pediatric studies have focused on evaluating the relationship between ABPM parameters with target organ changes in the heart, arterial wall, kidneys, and central nervous system. Cardiac changes, including left ventricular hypertrophy and left ventricular mass index, are among the most assessed target organ changes. Left ventricular hypertrophy is an established risk factor for cardiovascular events in adults [26]. There have been pediatric studies demonstrating that left ventricular mass increases with increasing BP [27, 28]. It has also been demonstrated that left ventricular mass index correlates with ambulatory systolic BP and systolic BP load in children [29]. Left ventricular mass index has also been found to be associated 24-h ambulatory systolic BP in obese children [30]. Increased cIMT is an established risk factor for strokes in adults [31]. There are multiple studies demonstrating an association between abnormal ABPM parameters and increased cIMT in children [32, 33]. Although obesity is associated with increased cIMT in children, several ABPM parameters have also been demonstrated to correlate with cIMT in an age-, gender-, and body mass index-matched study [34, 35].

In adults, hypertension is associated with poorer cognitive performance, psychomotor, and perceptual abilities [36]. Chronic, uncontrolled hypertension predicts cognitive decline over time [37]. In children, elevated office systolic BP is associated with lower test scores, which is a measure of short-term memory, attention, and concentration [38]. It has also been shown that children with ABPM confirmed untreated primary hypertension had lower performance on neurocognitive testing, especially measures of memory, attention, and executive function, compared to normotensive controls [39]. ABPM has also been found to be superior to office BP in distinguishing hypertensive children with lower neurocognitive test performance [40•]. ABPM can provide a more complete characterization of BP, showing a closer association with hypertension outcomes.

White Coat Hypertension

White coat hypertension (WCH) is defined as office BP ≥ 95th percentile and a mean ambulatory BP < 95th percentile with BP load < 25% on ABPM. WCH is common with a prevalence up to half of the children with an elevated office BP [41, 42]. While the clinical significance of WCH is unclear, there is increasing evidence that WCH may represent a pre-hypertensive state. In adults, it has been shown that patients with WCH had higher rates of cardiovascular morbidity and mortality compared to normotensive patients. In a recent meta-analysis, adult patients with untreated WCH were noted to have a markedly increased risk for cardiovascular events and all-cause mortality compared to those with normal BP [43]. No association was noted among those with treated WCH [43]. This risk was reduced when patients with WCH were treated [44]. There is also evidence that patients with WCH are at greater risk of developing sustained hypertension. In the PAMELA study, 43% of adult patients with WCH progressed to essential hypertension at follow-up 10 years later [45]. Similarly, in a Finnish study with an 11-year follow-up demonstrated 52% of adult patients with WCH progressed to essential hypertension compared to 12% of normotensive patients [46].

In children, fewer studies have been performed. Left ventricular hypertrophy has been evaluated among those with WCH. Most studies have suggested risk for left ventricular hypertrophy does not differ between WCH and normotensive patients, but the left ventricular mass index may be an intermediate between normotensive and hypertensive children after accounting for body mass index [47–49]. Myocardial performance index, a global measure of systolic and diastolic ventricular dysfunction, has been compared in patients with WCH and essential hypertension. Although most of the study population ($N = 66$) was found to have normal myocardial performance index values, 7% of those with WCH had an abnormal value, suggesting that with an increased sample size, significant differences may be identified [50]. Increased cIMT has been noted in some studies of children with WCH, but not others [41, 51, 52]. Vascular stiffness, measured by pulse wave velocity, has not been found to be different in children with WCH compared to normotensives [41].

Significant variability in practice habits regarding a diagnosis of WCH was found in a survey of nephrologists [53]. Forty-nine percent recommended follow-up in 6–12 months, while 41% recommended no further follow-up. Although most utilized ABPM for diagnosis (93%), repeat ABPM was not routinely used for monitoring. Only half reported recommending a repeat ABPM in 1 to 2 years or as indicated. The Clinical Practice Guideline recommends ABPM to be performed in children with suspected WCH and repeat ABPM to be performed in 1–2 years in children with confirmed WCH [9•].

Masked Hypertension

Masked hypertension (MH) is defined as office BP < 95th percentile and a mean ambulatory BP ≥ 95th percentile with BP load ≥ 25% on ABPM. The prevalence of pediatric MH ranges from 5 to 11% and increases to 35–50% in those with risk factors for hypertension, such as chronic kidney disease and coarctation of the aorta [54–57]. Compared to normotensive children, children with MH have been found to have a higher left ventricular mass index and increased cIMT [41, 58]. In addition, obese children are at higher risk to develop MH compared to lean children [59]. MH is also strongly associated with secondary hypertension. In conditions associated with MH, ABPM placement should be considered annually to identify those with hypertension and to ultimately reduce their cardiovascular risk factors (these conditions are discussed in further detail below).

Secondary Hypertension

Children with secondary hypertension are more likely to present at a younger age and have an increased daytime systolic BP load and increased daytime and nighttime diastolic BP, making ABPM useful for management. Patients with secondary hypertension are at increased risk of hypertensive end-organ damage. Utility of ABPM in specific populations with secondary hypertension as well as ABPM recommendations are discussed in detail below. ABPM rationale and suggested frequency for each indication are summarized in Table 2.

Chronic Kidney Disease

Hypertension affects 50% of children with chronic kidney disease [60]. It is important that hypertension is recognized in children with chronic kidney disease, as hypertension is a modifiable risk factor for progression of renal disease [60, 61]. Hypertension in this population can be missed due to an increased risk of MH compared to the general population [56]. In a cross-sectional study, 38% of subjects with chronic kidney disease were found to have MH [56]. Additional research has demonstrated that elevated BP is associated with the presence of abnormal subclinical markers of cardiovascular disease, including increased cIMT and left ventricular mass index [62]. ABPM has been shown to more effective at monitoring BP in the chronic kidney disease population than office BP [61]. Tighter BP control with intensified ABPM-guided hypertension management has been shown to increase renal survival [61]. It is important to include ABPM for recognition and monitoring of hypertension to slow progression of chronic kidney disease and reverse early cardiovascular disease. ABPM should be performed annually in patients with chronic kidney disease to evaluate for hypertension, as well as BP control.

Renal Transplantation

Similar to chronic kidney disease, children with renal transplant have a high prevalence of hypertension. There is an increased prevalence of MH, around 25–45% [63]. In addition, among treated patients, ABPM revealed 53% with uncontrolled hypertension, stressing the importance of routine use of ABPM [63]. Improved BP control guided by ABPM resulted in the normotensive group to have stable allograft function 2 years following transplant, while the hypertensive group had a significant decline in function [63]. In contrast, a more recent study with a small sample of 23 patients identified that targeting ambulatory BP to < 50th percentile is not associated with slowing the progression of chronic allograft dysfunction in children after renal transplant [64]. As was noted in patients with chronic kidney disease, ABPM appears to be important for not only, identification of hypertension, but also for management of their hypertension to potentially preserve their allograft function. Analogous to chronic kidney disease, ABPM should be performed annually.

Non-Renal Solid Organ Transplantation

Although hypertension has been reported to be significantly higher than the general pediatric population following liver, intestinal, and cardiac transplantation [65–68], there is limited data regarding ABPM use in these populations. The prevalence of MH has also been demonstrated to be higher in cardiac and liver transplant patient than renal transplant recipients [67]. Office BP has been found to poorly correlate with ABPM parameters [69, 70]. Annual ABPM is recommended for accurate diagnosis of hypertension in post-transplant recipients.

Table 2 Conditions in which ambulatory blood pressure monitoring is useful

Condition	Rationale	Frequency
Primary HTN evaluation		Perform if elevated BP > 1 year or stage 1 HTN at 3 clinic visits
White coat HTN evaluation		Consider repeating in 1–2 years
Secondary HTN	Severe HTN, nocturnal HTN, MH	Perform annually
Chronic kidney disease	Nocturnal HTN, MH	Perform annually
Diabetes (type 1 and type 2)	Nocturnal HTN, MH	Perform annually
Solid organ transplant	Nocturnal HTN, MH	Perform annually
Obstructive sleep apnea	Non-dipping	Perform annually
Coarctation of the aorta	MH	Perform annually starting no more than 12 years following repair
BP medication management	Confirm BP control	Perform every 1–2 years

HTN, hypertension; MH, masked hypertension; BP, blood pressure

Coarctation of the Aorta

Coarctation of the aorta is a common cause of secondary hypertension, representing about 3% of pediatric hypertension [71]. Nocturnal hypertension and MH can recur years following coarctation repair [72]. Persistent aortic hypoplasia has been noted in 48% of repaired patients with sustained hypertension in 42% [73, 74]. Ambulatory hypertension has been noted in 62% of patients an average of 18 years following repair, even though their aortic arches were normal [75]. ABPM is a critical tool for following BP in coarctation of the aorta patients following repair and should be considered for routine use. It has been recommended that ABPM be performed no less than 12 years following coarctation of the aorta repair and then annually [9•, 76].

Type 1 and 2 Diabetes

The prevalence of hypertension in children with type 1 diabetes is reported to be between 6 and 16%, which is frequently unrecognized and untreated [77]. Children with diabetes were found to have higher systolic and diastolic BP compared to controls [78]. In addition, abnormal Doppler echocardiographic indices were associated with elevated BP loads, suggesting early diastolic dysfunction [78]. Nocturnal hypertension, frequently seen in conjunction with type 1 diabetes, is associated with diabetic nephropathy and end-organ damage [79]. Patients with diabetic complications, defined as microalbuminuria and diabetic retinopathy, had significantly elevated nighttime mean arterial pressure and diastolic BP compared to patients without complications [80]. ABPM may be an important tool in following these patients and reducing their risk of cardiovascular events.

In contrast to type I diabetes, there have been few studies evaluating ABPM use in type 2 diabetes. A study of adolescents with type 2 diabetes found decreased nocturnal dipping and elevated mean systolic 24-h, daytime, and nighttime BP compared to controls [81]. A prospective cohort study is currently underway, which is assessing risk factors, including ABPM parameters, for diabetic kidney disease in adolescents with type 2 diabetes [82]. Their preliminary analysis identified an association between hypertension and albuminuria in adolescents with type 2 diabetes, which has not been previously identified [83]. This finding suggests consideration of ABPM use annually in children with type 2 diabetes.

Obstructive Sleep Apnea

Obstructive sleep apnea is one of the more common comorbidities of obesity. Compared to children who were primary snorers, children with moderate-to-severe obstructive sleep apnea were found to have higher ABPM parameters, including nighttime systolic BP and mean arterial pressures [84]. In a study evaluating neurobehavioral and cognitive function found lower measures of function in hypertensive adolescents with obstructive sleep apnea compared to hypertensive adolescents without obstructive sleep apnea [85]. In otherwise healthy children with sleep-disordered breathing, ABPM parameters, including blood pressure load and 24-h mean BP, were significantly increased suggesting sleep-disordered breathing has a role in cardiovascular morbidity [86]. ABPM following tonsillectomy has improved some ABPM parameters, suggesting that improvement of obstructive sleep apnea contributes to lowering of BP [87, 88]. Frequent BP monitoring via annual ABPM may assist in the detection of hypertension and eventual prevention of cardiovascular consequences.

ABPM Limitations

There are limitations for pediatric ABPM. The ABPM reference data are based on values from the German Working

Group on Pediatric Hypertension, which evaluated children aged 5 to 20 years [16]. The children included in this evaluation are a homogenous Caucasian central European population, which is likely not generalizable to children of different races, suggesting that normative data based on a larger and more diverse population is needed.

ABPM equipment is not universally available in pediatric clinics. A single ABPM monitor along with its software costs around $3500–$4000. Many government-based and other private health insurances do not cover or have very low reimbursement rates for pediatric ABPM. It is estimated that 190–200 ABPM studies would need to be performed to recover the initial starting cost for each monitor purchased [37]. Additionally, there are adolescent patients where even adult ABPM cuffs are too small and will not fit appropriately. For this subgroup of children, ABPM cannot reliably be performed. Improved availability of monitors and associated equipment, such as larger cuff sizes, is vital in ABPM becoming a routine part of BP evaluation and management.

Summary

Diagnosis and management of hypertension by ABPM are critical in the prevention and delay of cardiovascular complications of hypertension. Pediatric ABPM studies have demonstrated superiority over office BP in identification of target organ outcomes. In addition, ABPM has been shown to be associated with disease progression, suggesting that routine use of ABPM may be able to slow worsening of disease. ABPM is necessary to identify WCH, MH, and nocturnal hypertension. Without ABPM use in these patients, their hypertension would not be recognized and able to be managed, which would ultimately increase their risk of cardiovascular consequences.

Compliance with Ethical Standards

Conflict of Interest The authors declare no conflicts of interest relevant to this manuscript.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

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