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Ambulatory Blood Pressure Monitoring Tolerability and Blood Pressure Status in Adolescents: the SHIP AHOY Study

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Abstract

Ambulatory blood pressure monitoring (ABPM) provides a more precise assessment of blood pressure (BP) status than clinic BP and is currently recommended in the evaluation of elevated BP in children and adolescents. Yet, ABPM can be uncomfortable for patients and cumbersome to perform. We evaluated the tolerability of ABPM in 232 adolescent participants (median age 15.7 years, 64% white, 16% Hispanic, 53% male) in the Study of Hypertension In Pediatrics Adult Hypertension Onset in Youth (SHIP AHOY) and its potential effects on ABPM results.

Ambulatory BP status (normal vs. hypertension) was determined by sex and height-specific pediatric cut-points. Participants were asked to rank their wake and sleep tolerability to ABPM from 1 (most tolerant) to 10 (least tolerant); those with tolerability of 8 were considered ABPM intolerant. Forty-three participants (19%) had wake ambulatory hypertension (HTN), 42 (18%) had sleep ambulatory HTN, and 64 (28%) had overall (wake and/or sleep) ambulatory HTN. Forty participants (17%) were intolerant to ABPM during wake hours, and 58 (25%) were intolerant during sleep. ABPM intolerance during wake, but not sleep, hours, was independently associated with wake (OR 2.34, CI 1.01–5.39) and overall (OR 2.94, CI 1.21–7.18) ambulatory HTN. In conclusion, poor tolerability to ABPM is associated with a higher prevalence of ambulatory HTN in adolescents, and should be taken into consideration at time of ABPM interpretation.

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Conflicts of Interest

No conflicts of interest were declared.

Keywords

hypertension; adolescents; ambulatory blood pressure monitoring

Introduction

Ambulatory BP (ABP) is a more robust measure of BP status compared to clinic BP, has stronger association with target organ damage (TOD) in both adult (1, 2) and pediatric (3–9) populations, and is currently recommended (10) for confirmation of hypertensive status in children and adolescents.

During ABP monitoring (ABPM), patients are required to wear a BP cuff connected to a small recording device for 24 hours, and to remain still every 20–30 minutes during BP measurement, including during sleep. The procedure may not be well tolerated by some patients, and may potentially affect the successful performance of ABPM. Studies in adults indicate that ABPM is a relatively less favored option of BP monitoring for many patients (11, 12), due to disturbance of both sleep and regular daily activities, and that it is sometimes painful (11, 13, 14). Patients with poor sleep quality during ABPM were shown to have higher prevalence of abnormal dipping (15), and weaker association of ABPM results with outcomes (16). Although there are some data regarding children's acceptance and tolerance of ABPM, little is known about its association with ABPM results (17–21).

The Study of Hypertension in Pediatrics Adult Hypertension Onset in Youth Study (SHIP AHOY) is a cross-sectional cohort study designed to determine BP levels and phenotypes (using both in-clinic + ABPM measurements) that predicts BP related TOD in adolescents (22). The present report includes the first 232 participants in this cohort who reported their tolerability of ABPM and explores the tolerability in these adolescents to ABPM, and its potential effects on ABPM results.

Methods

Population

The rationale and design of the SHIP AHOY study are detailed elsewhere (22). The study recruited otherwise healthy adolescents across a wide range of BP percentiles, including healthy volunteers or referred patients. By design, the SHIP AHOY participants are divided in either low-risk BP (clinic systolic BP (SBP) <75th percentile, mid-risk SBP (80th - <90th percentiles) or high-risk SBP (≥90th percentile) categories. The study was initiated prior to the publication of the 2017 American Academy of Pediatrics (AAP) clinical practice guideline (CPG) (10); therefore, BP stratification at enrollment is based on the 2004 Fourth Report (23) BP tables. The criteria for participation in the study were 11–19 years of age, excluding: pregnant or breast-feeding females; symptomatic stage 2 HTN; use of antihypertensive medication within the past 6 months; receiving metformin and lipid-lowering agents; or medications known to affect BP, including glucocorticoids, calcineurin inhibitors, and oral decongestants. Patients were also excluded if they had any medical

condition known to be associated with the potential for elevated BP, such as diabetes, or any form of heart or kidney disease.

Data Collection

On enrollment, demographic (age, sex, race, ethnicity) and medical history information were collected; weight and height were measured. The study protocol had institutional review board (IRB) approval. Written informed consent/assent was obtained from all enrolled participants according to local IRB requirements.

BP Measurements

Clinic BP status was determined based on the average of 6 BPs obtained by auscultation over two visits 1–2 weeks apart, measured according to a standardized method according to accepted criteria (10, 23). Cuff size was guided by measurement of the mid-upper arm circumference. The BP was taken in the seated position in the right arm, resting at heart level, after 5 minutes of rest with an aneroid sphygmomanometer (Mabis Medic-Kit3, Healthsmart, Lubbock, TX). Each site's personnel received standardized training in BP measurement. BP was measured 4 times at 2 minute intervals on each of the two visits, discarding the first measurement on each occasion. The mean of the six remaining BP measurements was used in analysis.

Ambulatory BP was measured with the OnTrak 90227 device (SpaceLabs™, Snoqualmie, WA). Using the arm circumference measurement obtained as part of the auscultatory BP measurement, a properly sized cuff was selected and the monitor placed on the participant. Three resting BP's were obtained immediately after monitor placement to confirm correct placement and function of the monitor. For each 26-hour recording, measurements were obtained every 20 minutes through the day and night. Participants received a form in which they kept a diary to record time to sleep, time of waking, and timing of any napping. Diary data were used to divide the ABPM studies into accurate sleep-wake periods. No hours of monitoring were discarded, consistent with current AHA recommendations for pediatric ABPM (24). The form also included the following questions: (1) for either day or night times (figure 1): "On a scale of 1 (not at all) to 10 (all the time), how much did the monitor bother you or interrupt your activities/sleep?"; (2) "Did you experience any activities during monitoring that might raise your blood pressure (strenuous activity, pain, stressful situation)?" During the research visit in which ABPM was placed, a research coordinator went over these questions, and examples of activities that might affect BP were given. For the purpose of this analysis, if the response to the two latter questions was ≥ 8 , the participant was considered intolerant to the ABPM for that time period. This cut point was selected in reference to pain scoring scales in which severe pain is usually defined as ≥ 7 –8/10 (25). A small, IRB-approved payment was provided to participants at the completion of the ABPM study.

Ambulatory BP (ABP) Status Classification

ABPM was analyzed based on the AHA recommendations for pediatric ABPM (24), using pediatric normative ABPM data obtained with the same device (26): 1) Normal ABP: mean 24 hour SBP/DBP, and both wake and sleep BP $< 95^{\text{th}}$ percentile for sex and height; 2)

Ambulatory HTN: mean 24 hour SBP/DBP, or wake/sleep BP 95th percentile for sex and height. ABP index was calculated as the mean measured BP divided by the 95th percentile for sex and height, meaning that patients with normal ABP had ABP index <1, while ambulatory HTN was defined as ABP index of ≥ 1 (27).

Statistical analysis

For descriptive statistics, categorical variables are presented as percentages and continuous variables are presented as median (IQR). Association between categorical variables was done using chi square/Fischer's exact testing, and between continuous variables using Wilcoxon signed-rank test/t test. Logistic regression was used to investigate the independent association of ABPM intolerability with ambulatory HTN. All variables associated with ambulatory HTN in univariate analyses ($p < 0.15$) were initially included in the model. These included non-white race, sex, BMI percentile, and arm circumference. Backward elimination was performed to determine variables included in the final model, with an inclusion criterion of P less than 0.05. Odds ratios (ORs) were reported for each independent predictor along with Wald 95% confidence intervals (95% CIs). All statistical analyses were performed using SAS 9.3 statistical software (SAS Institute Inc, Cary, NC)

Results

Study Population

Two hundred and thirty three participants (median age 15.7 years (IQR 14.4–16.9), 53% male, 64% white, 16% Hispanic) with ABPM results who ranked their ABPM tolerability were included in this analysis. Patient characteristics are presented in table 1. Our study population was overweight, with median BMI percentile of 91. Median duration of ABPM was 26 hours (IQR 25.6–26.7), median number of successful readings was 73 (IQR 66–77), and median rate of successful readings was 87% (IQR 77–92). In three cases nocturnal ABP data was missing. Two hundred and nineteen participants responded to the question regarding activities potentially raising their blood pressure, among them 91 (42%) reported such activities. Thirty-four (15%) and 25 (11%) participants had wake systolic and diastolic HTN, respectively, while 33 (14%) and 28 (12%) had sleep systolic and diastolic HTN. Combining systolic and/or diastolic HTN, 43 participants (19%) had wake ambulatory HTN, 42 (18%) had sleep HTN, and 64 participants (28%) had overall (systolic and/or diastolic, wake and/or sleep) ambulatory HTN.

ABPM Tolerability

Median wake tolerability score was 4 (IQR 2–7), with 40 (17%) participants being intolerant to ABPM. Median sleep tolerability score was also 4 (IQR 2–8), but more patients 58 (25%) were intolerant during sleep compared to wake hours ($p = 0.009$). Overall, 73 participants (32%) were intolerant while awake, and/or during sleep, among them 25 (11%) were intolerant to ABPM during both periods. Characteristics of ABPM tolerant and intolerant participants are shown in table 2. ABPM intolerant participants had higher weight, BMI, BMI percentile, and arm circumference. These parameters were the highest in participants intolerant to ABPM during both wake and sleep (data not shown). Intolerant participants during sleep were slightly older and taller, while more intolerant participants during wake

hours were black. Intolerant participants during wake hours were also more likely to report “potentially raising BP activities” than tolerant ones (59% vs. 38%, $p=0.03$). Sixteen participants had a sleep period shorter than 6 hours – among these participants, 44% had poor sleep ABPM tolerability, compared to 24% of those with longer sleep periods. This association, however, was not statistically significant ($p=0.07$). We found no association between late bedtime (post-midnight) and sleep ABPM tolerability.

ABPM Tolerability and ABP Status

Compared to tolerant participants, intolerant participants had a significantly lower median number of successful BP readings (70 vs. 74, $p=0.01$) and lower ABPM reading success rate (82% vs. 88%, $p=0.006$, Figure 2). There was no difference in ABPM duration between the groups.

Association between ABPM tolerability and ABP status is presented in table 3. Participants intolerant to ABPM during wake hours had significantly higher prevalence of wake as well as overall (wake and/or sleep) ambulatory HTN. In a multiple regression analysis poor wake ABPM tolerability remained independently associated with wake (systolic and/or diastolic) HTN (OR 2.34, CI 1.01–5.39, $p=0.046$), systolic (wake and/or sleep) HTN (OR 3.36, CI 1.34–8.44, $p=0.01$), diastolic (wake and/or sleep) HTN (OR 2.40, CI 1.08–5.31, $p=0.03$), and overall (systolic and/or diastolic, wake, and/or sleep) ambulatory HTN (OR 2.94, CI 1.21–7.18, $p=0.02$). Participants with poor sleep tolerability were slightly more likely to have sleep HTN and nocturnal systolic dipping $<10\%$ (40% vs. 33%), but this difference was not statistically significant. We did not observe any association of ABPM tolerability with diastolic nocturnal dipping.

Discussion

In this cohort of otherwise healthy adolescents, we were able to demonstrate the association between patient’s tolerance to ABPM and ABPM results. Specifically, our findings show that 32% of our study population were significantly disturbed by the monitoring during wake and/or sleep hours, affecting the number and rate of successful readings. These results are consistent with previously published data in both adults and children regarding intolerance to ABPM, especially during the night (11–14, 17–19). We also observed that participants intolerant to ABPM were more likely overweight and have higher arm circumference than tolerant ones. This may reflect more discomfort during cuff inflation. Of note, an early report on difficulties with ABPM in children and adolescents showed that high BMI was independently associated with increased number of nonsense readings (28).

We were also able to show that intolerance to ABPM was associated with a higher prevalence of ambulatory HTN. There are few data available regarding the association between ABPM tolerability and ABP status, mostly studying the effect of sleep quality on ABP. One adult study reported that better sleep quality during ABPM was associated with greater nocturnal dipping (15), while another study reported that patients with poor ABPM tolerability were more likely to have elevated 24-hour BP (14). In our study, however, participants with poor wake ABPM tolerability only had higher prevalence of wake and

overall (wake and/or sleep) HTN, and we did not observe any significant association between sleep ABPM tolerability and ABP status.

One potential explanation of the association between poor ABPM tolerability and ambulatory HTN is that the elevated BP of patients intolerant to ABPM is at least partly related to their discomfort during ABPM. In such case, using a more tolerable method of BP monitoring might result in a different BP status. Of note, a study by Verdecchia et al. (16) demonstrated that the prognostic value of nighttime BP for future cardiovascular events disappeared in adult patients with perceived sleep deprivation 2 hours during ABPM, suggesting that nocturnal BP levels in these patients were affected by their poor ABPM tolerability. On the other hand, hypertensive patients, who require more inflation of the BP cuff, and who are relatively overweight with higher arm circumference might be more disturbed by ABPM. In this case, poor ABPM tolerability is just a reflection of the true BP status. Given that intolerant participants more frequently reported BP raising activities, another explanation may be that these activities affected both these participants' tolerability and ABP. As our study was cross-sectional we cannot prove causality, and more research is required on that matter.

Our study has several other limitations. Our population was relatively overweight and hypertensive, and although they may represent the typical adolescent population referred to hypertension evaluation (29, 30), our results may not apply to the general adolescent population. Our only assessment of ABPM tolerability was the participant's ranking, and we do not have more data regarding specific bothersome components of the "ABPM experience" that might have affected the ABPM results. Furthermore, our tolerability score was not validated prior to or during the study, therefore we cannot comment regarding its reliability or reproducibility. Our study size may be too small to characterize ABPM intolerant hypertensives and any effect of ABPM intolerance on the association of BP status and end-organ damage, as this group contained just 32% of the total cohort analyzed. In our study, BP was measured in 20 minutes intervals during both wake and sleep, whereas in many practices, BP is measured every 30 minutes during sleep. It is possible, that less frequent nighttime measurements would result in better tolerability to ABPM. Finally, our sample consisted of voluntary participants in a research study who received a financial incentive for wearing the monitor. This incentive might have affected their tolerability ranking, and/or their decision not to remove the monitor.

In summary, our study showed that a substantial number of adolescents undergoing ABPM tolerated it poorly and had higher BP compared to those with good tolerability. Physicians need to take tolerability into consideration when interpreting ABPM in adolescents, particularly in those who are overweight.

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On a scale of 1 (not at all) to 10 (all the time), how much did the monitor bother you or interrupt your activities/sleep:

DAY: ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10
not a bother *bothered a lot*

NIGHT: ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10
slept well *slept very poorly*

Figure 1–.

A question regarding tolerability to ABPM as appeared in the form given to study participants before ABPM initiation.

Figure 2–.

Association of poor wake and/or sleep ABPM tolerability with ABPM quality: (A) ABPM duration; (B) number of successful readings; and (C) rate of successful readings.

Table 1-

Study Population Characteristics (n=232)

Demographic and Anthropometrics	
Age, y	15.7 (14.4–16.9)
Male Sex (%)	124 (53)
Race (%)	
White	148 (64)
Black	55 (24)
Asian	11 (5)
Other	18 (8)
Hispanic (%)	37 (16)
Height (m)	1.68 (1.61–1.75)
Weight (Kg)	73.3 (59.3–92.3)
BMI (kg/m ²)	25.6 (22.0–31.8)
BMI Percentile	91.0 (66.2–98.2)
Arm Circumference (cm)	29 (26–34)
Clinic BP	
Clinic SBP (mmHg)	122 (113–130)
Clinic SBP Percentile	84 (59–93)
Clinic DBP (mmHg)	81 (73–87)
Clinic DBP Percentile	94 (75–98)
Ambulatory BP	
Mean day SBP	122 (114–129)
Mean Wake SBP Index	0.91 (0.86–0.97)
Systolic Wake HTN, n (%)	34 (15)
Mean day DBP	70 (66–76)
Mean day DBP index	0.85 (0.80–0.92)
Diastolic Wake HTN, n (%)	25 (11)
Mean sleep SBP	107 (100–113)
Mean sleep SBP Index	0.90 (0.85–0.96)
Systolic Sleep HTN, n (%)	33 (14)
Mean sleep DBP	56 (53–61)
Mean sleep DBP Index	0.85 (0.80–0.92)
Diastolic Sleep HTN, n (%)	28 (12)
SBP night dip	11.8 (7.8–16.4)
SBP nocturnal dip <10%, n (%)	79 (35)
DBP night dip	18.5 (14.1–24.3)
DBP nocturnal dip <10%, n (%)	31 (13)

Table 2–

Characteristics of ABPM tolerant and intolerant participants

	Wake (n=232)		Sleep (n=231) ^a	
	Tolerant (n=192)	Intolerant (n=40)	Tolerant (n=173)	Intolerant (n=58)
Age	15.7 (14.3–16.9)	15.9 (14.6–17.1)	15.6 (14.1–16.8)	16.3 (15.3–17.1) ^b
Male Sex (%)	106 (55)	18 (46)	94 (54)	29 (51)
Race (%)				
White	129 (68)	20 (51)	113 (66)	34 (61)
Black	41 (22)	14 (36) ^c	41 (24)	14 (25)
Asian	10 (5)	1 (3)	10 (6)	1 (2)
Other	10 (5)	4 (10)	7 (4)	7 (12)
Hispanic (%)	30 (16)	7 (18)	25 (14)	12 (21)
Height (m)	1.67 (1.60–1.74)	1.69 (1.64–1.77)	1.67 (1.60–1.74)	1.71 (1.64–1.77) ^b
Weight (Kg)	71.5 (57.8–88.1)	83.2 (67.8–113.6) ^b	70.5 (57.3–86.3)	83.2 (72.5–114.0) ^b
BMI (kg/m²)	25.4 (21.8–30.7)	29.4 (23.4–38.4) ^b	25.2 (21.5–29.6)	31.4 (23.4–37.0) ^b
BMI Percentile	90.1 (66.0–97.6)	98.0 (82.5–99.0) ^b	88.7 (66.0–97.1)	96.4 (82.5–99.2) ^b
Arm Circumference (cm)	29 (25–33)	34 (28–38) ^b	29 (25–33)	34 (29–39) ^b
SBP (mmHg)	121 (112–130)	123 (115–130)	121 (113–129)	126 (113–131)
SBP Percentile	84 (55–93)	85 (72–94)	84 (59–92)	86 (54–95)
DBP (mmHg)	81 (72–87)	81 (75–86)	81 (73–87)	80 (74–85)
DBP Percentile	93 (75–98)	94 (79–98)	94 (76–98)	92 (77–98)

^a one patient had missing sleep tolerability data^b <p<0.05 compared with ABPM tolerant^c p=0.06 compared with ABPM tolerant

Table 3–

Prevalence of Ambulatory Hypertension in Tolerant and Intolerant (tolerability score = 8) Participants

	Systolic		Diastolic		Systolic and/or Diastolic	
	Tolerant	Intolerant	Tolerant	Intolerant	Tolerant	Intolerant
Wake HTN (%)	24/192 (13)	10/40 (25) ^a	17/192 (9)	8/40 (20) ^a	30/192 (16)	13/40 (33) ^a
Sleep HTN (%)^b	20/171 (12)	12/57 (21)	19/171 (11)	9/57 (16)	28/171 (16)	13/57 (23)
Wake and/or Sleep HTN (%)^{b,c}	34/191 (18)	14/39 (36) ^a	30/191 (16)	12/39 (31) ^a	46/191 (24)	18/39 (46) ^a

^a p<0.05 compared with tolerant patients^b four patients had missing data regarding sleep BP/sleep tolerability^c according to wake ABPM tolerability