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Adherence to Antihypertensive Medications and Associations with Blood Pressure Among African Americans with Hypertension in the Jackson Heart Study (JHS)

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Abstract

The purpose of this study was to test the association between a self-report measure of 24-hour adherence to antihypertensive medication and blood pressure (BP) among African Americans. The primary analysis included 3,558 Jackson Heart Study participants taking antihypertensive medication who had adherence data for at least one study exam. Non-adherence was defined by self-report of not taking one or more prescribed antihypertensive medications, identified during pill bottle review, in the past 24 hours. Non-adherence and clinic BP were assessed at Exam 1 (2000–2004), Exam 2 (2005–2008), and Exam 3 (2009–2013). Associations of non-adherence with clinic BP and uncontrolled BP (systolic BP [SBP] ≥ 140 mmHg or diastolic BP [DBP] ≥ 90 mmHg) were evaluated using unadjusted and adjusted linear and Poisson repeated measures regression models. The prevalence of non-adherence to antihypertensive medications was 25.4% at Exam 1, 28.7% at Exam 2, and 28.5% at Exam 3. Non-adherence was associated with higher SBP (3.38 mmHg) and DBP (1.47 mmHg) in fully adjusted repeated measures analysis. Non-adherence was also associated with uncontrolled BP (prevalence ratio=1.26; 95% CI= 1.16–1.37). This new

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self-report measure may be useful for identifying non-adherence to antihypertensive medication in future epidemiological studies.

Keywords

hypertension; blood pressure; medication adherence; African Americans

INTRODUCTION

Hypertension is a leading modifiable risk factor for cardiovascular disease (CVD) in the United States and worldwide (1, 2). Among adults with hypertension, lowering blood pressure (BP) reduces the occurrence of myocardial infarction, stroke, and cardiovascular mortality (3, 4). African Americans have the highest prevalence of hypertension of any racial/ethnic group in the United States (1, 5). Despite similar rates of awareness and treatment of hypertension compared with whites, African Americans have a higher prevalence of uncontrolled BP (1, 5–7). Prior studies have consistently demonstrated that non-adherence to prescribed antihypertensive medication is more common among African Americans compared with whites (6), which may explain the lower prevalence of BP control (1, 7, 8).

The assessment of antihypertensive medication adherence is a substantial challenge in epidemiological research. Objective measures, including electronic monitoring, pharmacy refill records and pill counts, are considered the gold standard but are expensive and burdensome (9). Self-report measures have been validated against objective measures such as BP control and pharmacy refills (10–12), but are subject to recall and social desirability biases and tend to underestimate non-adherence (13). The use of self-report measures of medication adherence can be enhanced by providing a clear definition of non-adherence (e.g., not taking all medications vs. not taking some medications) and using a clearly defined time frame (e.g., non-adherence during the past 24 hours, past week, or past month) (14).

The primary aim of the current study was to test the associations between a self-report measure of medication non-adherence in the prior 24 hours and systolic blood pressure (SBP), diastolic blood pressure (DBP) and BP control. To address this aim, we analyzed data from the Jackson Heart Study (JHS), a prospective population-based cohort study comprised exclusively of African-American adults. If found to be associated with BP, self-reported 24-hour medication non-adherence may be a useful measure for future epidemiological studies.

METHODS

Overview

The JHS enrolled a community-based sample of 5,306 African American adults from the general population of the Jackson, MS metropolitan area and was designed to identify risk factors for CVD (15). The sample was composed of participants from the Atherosclerosis Risk in the Community (ARIC) site in Jackson, MS (30%) and a regionally representative sample of urban and rural residents from the Jackson, MS metropolitan tri-county region (Hinds, Madison and Rankin counties) that were randomly contacted (17%), were volunteers

(22%), or were secondary family members (31%). The study was approved by the institutional review boards of all participating institutions and all participants provided written informed consent at each study examination.

Measurements

Data were collected during three study visits in 2000–2004 (Exam 1), 2005–2008 (Exam 2), and 2009–2013 (Exam 3).

Antihypertensive Medication Use and Non-Adherence—Participants were asked to bring all prescribed and over-the-counter medications they had taken within the two weeks prior to each study visit (15). Study staff recorded the names of the medications and asked participants whether they had taken each medication in the past 24 hours. The following drug classes were coded as antihypertensive medication: aldosterone receptor antagonists, alpha blockers, angiotensin converting enzyme (ACE) inhibitors, angiotensin receptor blockers, beta blockers, calcium channel blockers, central acting agents, loop diuretics, potassium-sparing diuretics, thiazide diuretics, renin inhibitors, and direct acting vasodilators. Combination medications were separated into their individual classes. Participants were also asked whether they had taken antihypertensive medication in the two weeks prior to the exam. Those who self-reported antihypertensive medication use in the prior two weeks and had one or more antihypertensive medication classes identified during the pill bottle review were categorized as having treated hypertension.

Adherence was defined based on participants' reports of whether they had taken all prescribed antihypertensive medication in the 24 hours preceding the JHS exam. This follows recommendations to require full, rather than partial, adherence when using self-report measures categorizing adherence status to minimize the impact of underreporting of non-adherence (14). Participants who reported that they had not taken one or more of their prescribed antihypertensive medications were categorized as non-adherent. Non-adherence to antihypertensive medications was determined at each exam.

Blood Pressure—Clinic BP was measured at each study visit by trained staff after the participant had rested for at least 5 minutes. The right arm circumference was measured to determine the appropriate cuff size. Two BP measurements, one minute apart, were recorded and the mean SBP and DBP were calculated. Quality control procedures conducted by the JHS Coordinating Center included monitoring digit preference for each staff member and comparing mean BP measurements within and between staff. BP was measured at Exams 1 and 2 using a standard Hawksley random-zero sphygmomanometer (15). At Exam 3, SBP and DBP were measured using the Omron HEM907XL device. In addition, 2,228 participants at Exam 2 also had their clinic BP measured using the Omron HEM907XL device. A BP comparability study was conducted using simultaneous measurements of SBP and DBP from the Hawksley random-zero sphygmomanometer and Omron HEM907XL using a Y connector at Exam 2. SBP and DBP at Exam 1 were calibrated to the Omron device using robust regression as described previously (16). Additionally, for participants whose BP was only measured using the random-zero device at Exam 2, SBP and DBP at this

exam were calibrated to the Omron device. Uncontrolled BP at each exam was defined as mean clinic SBP ≥ 140 mmHg or mean clinic DBP ≥ 90 mmHg.

Covariates—Demographic, clinical, behavioral, and psychosocial characteristics as well as comorbid conditions associated with hypertension, uncontrolled BP or antihypertensive medication adherence were selected as covariates (17–21). Covariates included age, sex, body mass index (BMI), smoking status (current versus never/past smoker), education, employment status (full or part-time versus unemployed/retired), diabetes status, depressive symptoms, stress and perceived social support. BMI was defined by height and weight measured at each exam. As participants were not asked about smoking status at Exams 2 and 3, data collected during the annual follow-up telephone call most proximal to each exam were used to define current smoking status at these visits. Employment status at Exam 2 was also defined using this method. Education was reported in categories and continuous values were derived based on the methodology of Hickson, et al. (22). Diabetes status was defined at each exam by a self-reported prior diagnosis of diabetes or use of diabetes medications, fasting glucose ≥ 126 mg/dl, or HbA1c levels $\geq 6.5\%$. Depressive symptoms were measured using the Center for Epidemiologic Studies Depression scale (CESD-R). Scores on this 20-item scale ranged from 0 to 60 with higher scores indicating higher levels of depressive symptoms (23). Perceived stress was measured using the Weekly Stress Inventory (WSI), an 87-item inventory of minor daily stressors occurring over the prior week (24); ratings of perceived stressfulness of each endorsed stressor were summed to produce a measure of WSI impact (range 0–609). Perceived social support was measured using the Interpersonal Support Evaluation List, 16-item version (24); total scale scores range from 0–48, with higher scores indicating greater perceived support.

Study Population

Of the 5,306 participants enrolled in the JHS, 5,280 had complete clinic BP data and 5,138 also had pill bottle review data at Exam 1. Of these participants, 2,447 (47.6%) were taking antihypertensive medication and were included in the Exam 1 analysis sample. Of the 4,205 participants who completed Exam 2, 4,191 had complete clinic BP data and 4,189 also had pill bottle review data at Exam 2. Of these participants, 2,516 (60.0%) were taking antihypertensive medication and were included in the Exam 2 analysis sample. Of the 3,819 participants who completed Exam 3, 3,814 had complete clinic BP data and 3,808 also had pill bottle review data at Exam 3. Of these participants, 2,492 (65.4%) were taking antihypertensive medication and were included in the Exam 3 analysis sample. In total, 3,558 participants who were taking antihypertensive medication and had complete adherence data for one or more study exams were included in the primary repeated measures analysis.

Statistical Analysis

Characteristics of the study sample and mean clinic SBP and DBP were calculated overall and for adherent and non-adherent participants who were prescribed antihypertensive medication at each exam. The statistical significance of differences between adherent and non-adherent participants was determined using independent sample t-tests and chi-squared tests as appropriate. Using general linear repeated measures regression, we combined the data from Exams 1, 2 and 3 into a single longitudinal analysis to examine associations

between 24-hour non-adherence and BP. Repeated measures linear regression models were conducted to examine associations of non-adherence with SBP and DBP. Repeated measures Poisson regression models with robust covariance estimation were conducted to examine associations of non-adherence with the prevalence of uncontrolled BP. These analyses were performed on the sample of 3,558 participants who were diagnosed with hypertension, taking antihypertensive medication and had complete data on 24-hour adherence for at least one visit. The association between non-adherence status and SBP and DBP and uncontrolled BP was examined in unadjusted, partially adjusted (Model 1), and fully adjusted models (Model 2). Covariates in Model 1 included age, sex and number of antihypertensive medication classes being taken. Model 2 included the variables in Model 1 and BMI, smoking, education, employment and diabetes status.

Linear and Poisson regression models were conducted to determine the association between non-adherence and SBP and DBP and uncontrolled BP at each exam separately as sensitivity analyses. The analysis of Exam 1 contained an additional model (Model 3) adjusted for depressive symptoms, weekly stress and perceived social support. As these psychosocial factors were only assessed only at Exam 1, Model 3 was not included in the repeated measures model or analyses of Exams 2 and 3 or for the pooled analysis described above. Due to missing data for psychosocial covariates for 1,113 participants in the sample at Exam 1, we performed multiple imputation using full conditional specification (FCS) (25). Missing data did not differ by 24-hour adherence status. Sensitivity analyses were also conducted using non-calibrated BP values from Exams 1 and 2. Analyses were conducted using SPSS Version 22 (26).

RESULTS

Participant Characteristics

Of the 3,558 JHS participants included in the primary analysis, 964 (27.1%) reported not taking all of their prescribed antihypertensive medication in the past 24 hours and were categorized as non-adherent at their first recorded exam (Table 1). The average age was 60.4 years (SD 11.1 years) and 32.9% of participants were male. Participants who were non-adherent to antihypertensive medication were older, less likely to be smokers, had fewer years of education, less likely to be employed and were more likely to have diabetes than those who were adherent. In addition, non-adherent participants were more likely to be taking three or more classes of antihypertensive medication and were more likely to be taking loop diuretics and angiotensin receptor blockers. Participant characteristics for each of the three Exams are presented in Supplemental Tables 1–3.

Associations Between 24-hour Medication Adherence and BP

When pooling all three exams, non-adherence to antihypertensive medication in the past 24 hours was associated with a higher mean BP in unadjusted [3.92 (standard error =0.50) mmHg for SBP; $p<.001$ and 0.59 (SE= 0.27) mmHg for DBP; $p=.030$] and fully adjusted analyses [3.38 (SE= 0.52) mmHg for SBP; $p<.001$ and 1.47 (SE= 0.27) mmHg for DBP; $p<.001$] (Table 2). Non-adherence was also associated with higher prevalence of uncontrolled BP in both unadjusted (prevalence ratio [PR]= 1.28; 95%CI = 1.19–1.38; $p<.001$) and fully

adjusted analyses (PR= 1.26; 95%CI = 1.16–1.37; $p<.001$). The associations between 24-hour non-adherence and BP were present in cross-sectional analyses of Exam 1, even after adjustment for psychosocial covariates (Table 3). Sensitivity analyses at Exam 2 showed that 24-hour non-adherence was associated with SBP only in unadjusted analyses, with DBP only in adjusted analyses, and was not associated with BP control (Supplemental Table 4). At Exam 3, associations between 24-hour non-adherence and SBP, DBP and BP control were present after multivariable adjustment (Supplemental Table 5).

DISCUSSION

In the current population-based study of African Americans taking antihypertensive medication, between 25% and 30% of participants reported not taking their antihypertensive medication in the past 24 hours. Self-reported non-adherence to antihypertensive medications in the previous 24 hours was associated with higher BP levels (3.38 mmHg for SBP and 1.47 mmHg for DBP) and a higher prevalence of uncontrolled BP (26% higher prevalence in the non-adherent group compared to the adherent group) after multivariable adjustment. These associations were consistent across multiple study visits.

Participants who were non-adherent in the past 24 hours were prescribed more classes of antihypertensive medication, were more likely to take loop diuretics and angiotension receptor blockers, were older, were less likely to be smokers, had fewer years of education, were less likely to be employed, and were more likely to have diabetes. Age, sex, medication side effects, patient attitudes/beliefs about medication, quality of life, depression, social support, stress, financial issues and health care system issues have all been associated with medication adherence in previous studies (9, 27–31). Individual-level factors, particularly depression and younger age, have been more strongly related to non-adherence in African Americans than institution-level or provider-level factors (32). However, depressive symptoms and social support were not associated with non-adherence in the current study. It is possible that the factors influencing medication non-adherence in the previous 24 hours differ from the factors that contribute to usual patterns of non-adherence over weeks and months (33).

The 27% prevalence of non-adherence to antihypertensive treatment found using this new measure is comparable to the 20–40% non-adherence rates shown in previous research (29, 30, 34). In addition, the 26% higher prevalence of uncontrolled BP in the non-adherent sample from the repeated measures multivariable adjusted analysis is comparable to the 20–50% higher prevalence reported in previous studies (35). Associations between single-item medication adherence measures and disease biomarkers have been reported previously (36–38). However, to our knowledge, no prior studies have used a self-report measure of antihypertensive medication non-adherence assessed over the prior 24 hours.

A strength of the self-report measure of 24-hour non-adherence used in the current study is its specificity to both time and individual medications. A previous analysis of medication non-adherence in the JHS used a single item asking whether participants who reported taking antihypertensive medication had taken any of their BP medications in the past two weeks (39). All self-report measures of non-adherence are vulnerable to social desirability

(i.e., reporting being adherent to satisfy the interviewer), but defining adherence as having taken any versus all antihypertensive medications may further increase misclassification of non-adherence status (14). The current 24-hour non-adherence measure categorizes participants as adherent only if they reported taking all of their prescribed antihypertensive medication after being questioned about each medication individually. This method and the 24-hour reference frame may reduce the risk of recall bias, a limitation of most self-report adherence measures (12). On the other hand, the short reference period also raises the question of whether non-adherence in the past 24 hours is representative of an individual's typical medication taking behavior. While an assessment window of 30 days or less is recommended to reduce recall bias (14), 24 hours may be too brief. More research is required to examine how robust 24-hour non-adherence may be as a measure of adherence, especially in populations outside of the JHS.

Strengths and Limitations

Strengths of the current study include the large population-based sample of African Americans taking antihypertensive medication and the multiple assessments of non-adherence and clinic BP across three visits. This allowed us to run repeated measures analyses and replicate the associations between 24-hour non-adherence and clinic BP and BP control cross-sectionally at 3 study exams conducted over 14 years. The extensive data collection at each JHS exam also allowed us to control for demographic, clinical, behavioral and psychosocial factors. However, this study also has several limitations. First, gold-standard methods for assessing non-adherence to antihypertensive medication (e.g., urinary metabolites, pharmacy refill records, electronic monitoring) were not used. All self-report measures of non-adherence, including this 24-hour measure, likely underestimate non-adherence. It will be critically important to validate self-reported 24-hour non-adherence against well-established, objective measures in the future in order to establish its accuracy. Second, the JHS is an exclusively African American cohort and the findings related to 24-hour non-adherence may not generalize to other racial and ethnic groups. Third, there may be unmeasured confounders which influenced BP in addition to 24-hour non-adherence and the covariates utilized in the current analysis. Finally, more research is needed to understand patterns and effects of non-adherence over time, including discontinuation of antihypertensive treatment, a type of non-adherence that is not captured with this measure(40).

Conclusion

In summary, the present study demonstrates an association between self-reported 24-hour antihypertensive medication non-adherence and BP among African Americans. The prevalence of non-adherence estimated using this measure was consistent with prior studies and 24-hour non-adherence was associated with higher clinic BP and a higher prevalence of uncontrolled BP. These findings suggest that 24-hour non-adherence may be a useful measure for examining adherence in individuals taking antihypertensive medication.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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Highlights

- An assessment of 24-hour non-adherence to antihypertensive medications is proposed.
- African Americans from the multi-visit Jackson Heart Study (JHS) were the sample.
- The prevalence of 24-hour non-adherence was between 25–29% at three JHS exams.
- 24-hour non-adherence was associated with reduced blood pressure control.
- Results were consistent across three JHS examinations.

Table 1

Characteristics of Jackson Heart Study participants taking antihypertensive medication, overall and by 24-hour non-adherence status.

Characteristic	Overall (n=3,558)	Adherent (n=2,594)	Non-adherent (n=964)	p-value
Age	60.4 (11.1)	60.0 (11.0)	61.4 (11.3)	.001
Male, <i>n</i> (%)	1,172 (32.9%)	854 (32.9%)	318 (33.0%)	.971
Body mass index, kg/m ²	32.7 (7.3)	32.6 (7.3)	32.99 (7.3)	.159
Current smoking, <i>n</i> (%)	384 (10.9%)	302 (11.7%)	82 (8.5%)	.007
Years of education	13.5 (3.9)	13.6 (3.9)	13.1 (3.9)	.001
Employed, <i>n</i> (%)	1,622 (45.9%)	1,212 (47.0%)	410 (42.8%)	.026
Diabetes, <i>n</i> (%)	1,116 (33.4%)	794 (32.4%)	322 (36.1%)	.042
Number of prescribed antihypertensive medication classes, <i>n</i> (%)				
1	1,111 (31.2%)	840 (32.4%)	271 (28.1%)	.005
2	1,518 (42.7%)	1,111 (42.8%)	407 (42.2%)	
3	929 (29.7%)	643 (24.8%)	286 (29.7%)	
ACE inhibitor	1,365 (38.4%)	999 (38.5%)	366 (38.0%)	.766
Angiotensin receptor blocker	721 (20.3%)	504 (19.4%)	217 (22.5%)	.042
Beta blocker	752 (21.1%)	552 (21.3%)	200 (20.7%)	.729
Calcium channel blocker	1,266 (35.6%)	933 (36.0%)	333 (34.5%)	.430
Loop Diuretic	342 (9.6%)	218 (8.4%)	124 (12.9%)	<.001
Potassium-Sparing Diuretic	413 (11.6%)	295 (11.4%)	118 (12.2%)	.472
Thiazide Diuretic	1,970 (55.4%)	1,423 (54.9%)	547 (56.7%)	.315
Other antihypertensive medication	443 (12.5%)	293 (11.3%)	150 (15.6%)	.001

Note: Variables are presented with Mean (standard deviation) or as N (%). ACE = angiotensin converting enzyme.

Note: Characteristics reported for the participant's first included exam

Table 2

Associations between 24-hour non-adherence and clinic blood pressure measures across all examinations.

Variables	Adherent	Non-adherent	p-value
<i>Systolic blood pressure</i>			
Mean (SD), mm Hg	129.5(18.1)	133.3 (19.3)	<.001
	Difference (standard error)		
Unadjusted	0 (ref)	3.92 (0.50)	<.001
Model 1	0 (ref)	3.20 (0.49)	<.001
Model 2	0 (ref)	3.38 (0.52)	<.001
<i>Diastolic blood pressure</i>			
Mean (SD), mm Hg	74.5 (10.1)	75.1 (10.5)	.023
	Difference (standard error)		
Unadjusted	0 (ref)	0.59 (0.27)	.030
Model 1	0 (ref)	1.34 (0.25)	<.001
Model 2	0 (ref)	1.47 (0.27)	<.001
Uncontrolled Blood Pressure			
%	25.9%	33.2%	<.001
	Prevalence ratio (95% CI)		
Unadjusted	0 (ref)	1.28 (1.19–1.38)	<.001
Model 1	0 (ref)	1.22 (1.13–1.32)	<.001
Model 2	0 (ref)	1.26 (1.16–1.37)	<.001

Model 1 adjusted for age, sex and number of classes of antihypertensive medication prescribed.

Model 2 adjusted for age, sex, number of classes of antihypertensive medication prescribed, body mass index, smoking, education, employment and diabetes.

Uncontrolled blood pressure defined as systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mmHg.

Note: BP means and frequencies are reported across all study exams

Table 3

Associations between 24-hour non-adherence and clinic blood pressure at Exam 1.

Variables	Adherent (n=1,826)	Non-adherent (n=621)	p-value
<i>Systolic blood pressure</i>			
Mean (SD), mm Hg	130.2 (15.8)	135.1 (18.2)	<.001
	Difference (standard error)		
Unadjusted	0 (ref)	4.89 (0.76)	<.001
Model 1	0 (ref)	4.64 (0.75)	<.001
Model 2	0 (ref)	4.70 (0.75)	<.001
Model 3	0 (ref)	4.69 (0.76)	<.001
<i>Diastolic blood pressure</i>			
Mean (SD), mm Hg	75.6 (8.9)	76.3 (9.0)	.112
	Difference (standard error)		
Unadjusted	0 (ref)	0.66 (0.41)	.112
Model 1	0 (ref)	1.07 (0.38)	.005
Model 2	0 (ref)	1.19 (0.38)	.002
Model 3	0 (ref)	1.13 (0.38)	.003
<i>Uncontrolled blood pressure</i>			
N (%)	443 (24.3%)	220 (35.4%)	<.001
	Prevalence ratio (95% confidence interval)		
Unadjusted	1 (ref)	1.46 (1.24–1.72)	<.001
Model 1	1 (ref)	1.43 (1.22–1.68)	<.001
Model 2	1 (ref)	1.45 (1.23–1.71)	<.001
Model 3	1 (ref)	1.44 (1.22–1.69)	<.001

Model 1 adjusted for age, sex and number of classes of antihypertensive medication prescribed.

Model 2 adjusted for age, sex, number of classes of antihypertensive medication prescribed, body mass index, smoking, education, employment and diabetes.

Model 3 adjusted for age, sex, number of classes of antihypertensive medication prescribed, body mass index, smoking, education, employment, diabetes, depressive symptoms, stress and perceived social support.

Uncontrolled blood pressure defined as systolic blood pressure ≥ 140 mm Hg or diastolic blood pressure ≥ 90 mmHg.