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Research Article

Antihypertensive Use and Recurrent Falls in Community-Dwelling Older Adults: Findings From the Health ABC Study

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Abstract

Background. Despite wide-spread use of antihypertensives in older adults, the literature is unclear about their association with incident recurrent falls over time.

Methods. Health, Aging and Body Composition study participants (n = 2,948) who were well functioning at baseline (1997) were followed to Year 7 (2004). The main outcome was recurrent falls (≥2) in the ensuing 12 months. Antihypertensive use was examined as: (a) any versus none, (b) long- versus short-term (≥2 vs <2 years), and by (c) summated standardized daily dose (SDD; 1 = maximum recommended daily dose for one antihypertensive), and (d) subclass.

Results. Controlling for potential demographic, health status/behavior and access to care confounders, we found no increase in risk of recurrent falls in antihypertensive users compared to nonusers (adjusted odds ratio [AOR] = 1.13; 95% CI = 0.88–1.46), or those taking higher SDDs or for longer durations. Only those using a loop diuretic were found to have a modest increased risk of recurrent falls (AOR = 1.50; 95% CI = 1.11–2.03).

Conclusions. Antihypertensive use overall was not statistically significantly associated with recurrent falls after adjusting for important confounders. Loop diuretic use may be associated with recurrent falls and needs further study.

Key Words: Falls—Medication—Epidemiology—Drug related

Hypertension (especially systolic) is the most common chronic condition in older adults (1). If un- or undertreated, hypertension can increase risk of stroke, heart failure, and premature death (1). Numerous randomized controlled trials demonstrate the effectiveness of thiazide diuretics, central alpha blockers, renin-angiotensin-aldosterone system inhibitors, and calcium channel blockers in reducing blood pressure in adults well into their eighties (1). Even though these drugs are generally well tolerated, as few as 50% of elders with hypertension use antihypertensives (often more than one), and fewer than 50% of these have adequate blood pressure control (2,3).

Suboptimal blood pressure control may derive, in part, from concerns about adverse drug effects, including falls. Indeed, 18%–40% of community-dwelling elderly fall yearly (4–6), of whom nearly 50% have recurrent falls (6,7). Recurrent falls (as opposed to single falls) may be more clinically important as they may increase the risk of physician visits, functional status decline, nursing home admission, and death (6). To date only three studies have looked at the risk of antihypertensives and recurrent falls in community dwelling elders, and none of them demonstrated an increased risk after controlling for other important factors (8–10). None of these studies examined individual antihypertensive classes, dosage, or duration.

Thus, the objective of the current longitudinal study was to assess the association of overall and specific classes of antihypertensive use, dose, and duration with recurrent falls in community-dwelling, initially well-functioning elders.

Methods

Study Design, Data Source, and Sample

We used data from the Health, Aging, and Body Composition (Health ABC) study, a population-based, prospective, longitudinal observational study of community-dwelling older adults (11). This study was approved by the University of California at San Francisco (UCSF), University of Pittsburgh, and University of Tennessee Memphis Institutional Review Boards, and informed consent was obtained from each participant prior to data collection. The baseline sample (1997/1998) included 3,075 black and white men and women aged 70–79 years who reported no difficulty walking ¼ mile, or climbing 10 steps and lived in specified zip codes surrounding Pittsburgh, Pennsylvania and Memphis, Tennessee (11). Thus, the sample for the current analysis included 2,948 well functioning older adults at Year 1 with complete medication use and fall data the following year followed through Year 6 for antihypertensive medication exposure and Year 7 for recurrent falls.

Data Collection and Management

Participants were seen annually during a clinic or home visit and detailed physiologic (including blood pressure) and self-report questionnaire measurements (including demographics, health behavior/status (including medications), and access to health care factors were collected (11). Detailed medication data were collected in clinic or at home about products taken in the previous month using a state of the art "brown bag" review method (12,13). A similar data collection approach was used for telephone interviews if participants were unable to be seen in person. Studies have shown that medication use information collected by either "brown bag" or telephone methods are highly accurate and concordant with information about dispensed prescription drugs in claims data (14,15). For all medications, the interviewer recorded the name, strength, dosage form, and the number of dosage forms the respondents said they had used the previous day, week, or month. The medication data collected for the Health ABC Study were edited and coded using the Iowa Drug Information System (IDIS) Drug Vocabulary and Thesaurus (16). IDIS is a hierarchical coding system with eight character unique codes for specific drug ingredients, chemical and therapeutic categories. The therapeutic category code allows drugs to be assigned to 1 of 20 major therapeutic classes and 200 subclasses based on an expanded version of the American Hospital Formulary Services format (17).

Teleform was used to create scannable forms for direct data entry. Missing and questionable values were highlighted by the software for visual review and online editing. Additional range checks and data cleaning were conducted at the UCSF Coordinating Center. De-identified SAS permanent data files were created for analysis.

Primary Outcome

The number of falls in which the participant landed on the floor or ground in the previous 12 months was assessed at the year following medication use data collection (eg, Year 1 antihypertensive use and previous year falls reported at Year 2) for each wave (five waves). The primary outcome was recurrent falls (≥2) in the ensuing 12 months following report of medication use. This method of fall recall (in the previous 12 months) has been shown to be highly specific (91%–95%) in comparison with that reported using more frequent assessments (18).

Primary Independent Variable

Medications used to treat hypertension were grouped into therapeutic subclasses: (a) beta blockers; (b) alpha blockers (peripheral and central); (c) loop diuretics; (d) thiazide diuretics; (e) potassium-sparing diuretics; (f) calcium channel blockers; (g) angiotensin converting enzyme inhibitors; and (h) angiotensin receptor blockers (19). Too few participants were taking vasodilators so this class was not assessed. Any use was defined as the use of any medication from the eight subclasses. To evaluate the possibility of a dose–response relationship, the daily dose was calculated for current users for each individual antihypertensive medication by multiplying the number of dosage forms taken the previous day by the strength of the medication reported at the interview. The daily dose was then converted to a standardized daily dose (SDD) by dividing it by the *maximum effective dose* per day as noted in a standard reference (19). Thus, a person taking 1.0 standardized antihypertensive drug unit would have taken the maximum recommended effective daily dose for one agent. The standardized dose was summated for all antihypertensives, regardless of class, taken daily. Finally, to examine the impact of duration, long-term use was operationally defined as ≥2 years and short-term use as less than 2 years (19).

Control Variables

To address potential confounding, we controlled for a number of demographic, health status/behavior, and access to care factors (6,7). Demographic factors included age, sex, race, site, education (less than a high school education, high school graduate, and postsecondary education), and marital status (never married, married, and previously married).

Health behaviors included smoking status and alcohol use. Health status factors included pulmonary disease, arthritis, urinary problems, cerebrovascular disease, bodily pain in the previous month (13,19), vision (excellent/good sight, fair sight, and poor to

completely blind), and body mass index (underweight/normal, <24.9; overweight, 25.0–29.9; and obese, ≥30). Self-rated global health was dichotomized as excellent/very good/good versus fair/poor. In addition, time-varying covariates were created for depressive symptoms (Short Center for Epidemiologic Studies-Depression Scale >10), cognitive impairment (modified mini-mental state test [3MS] <80) and the total number of prescription medications (excluding dugs that increase falls, and antihypertensive drugs) per participant (7,20,21). Time varying exposure to any drug that increases the risk of falls (non-anticholinergic central nervous system medications, including benzodiazepines, antidepressants, antipsychotics, and opioids) was also assessed (7). Access to care factors included dichotomous variables for hospitalization in previous 12 months, private physician, prescription insurance, and flu shot in previous 12 months (3).

Self-reported hypertension was subdivided into controlled (<140/90 mmHg) and uncontrolled (≥140/90 mmHg) on a time-varying basis. Antihypertensives can be used for a number of comorbid conditions (1,22). Therefore, to mitigate potential confounding by indication, we included self-reported peripheral artery disease, benign prostatic hyperplasia symptoms, coronary heart disease, congestive heart failure, and diabetes.

Statistical Analysis

We used appropriate descriptive statistics for summarization and generalized estimating equations for eliciting the main findings (23–25). First, we assessed the unadjusted association between antihypertensive use and recurrent falls over time. Second, a priori covariates that may affect recurrent falls were included: site, heart failure, benign prostatic hypertrophy, cognitive impairment, depressive symptoms, self-reported hypertension (controlled/uncontrolled), and other drugs that increase the risk of falls. Each antihypertensive subclass was run as a separate model and controlled for antihypertensive subclass use other than the subclass being evaluated, with no use being the reference group. Finally, additional covariates were selected using a forward stepwise selection approach applied separately for each of three domains of covariates (demographic, health status/behavior, and access to health care). Specifically, stepwise detected covariates and those deemed important a priori were included in the final model. We also conducted sensitivity analyses by restricting the sample to only those with hypertension (whether controlled or uncontrolled) at baseline, and stratifying the analysis by any falls history and median gait speed at baseline. All analyses were conducted using SAS software (version 9.3; SAS Institute, Cary, NC).

Results

At baseline these well functioning participants had a mean (standard deviation) age of 73.6 (2.9) years, 51.6% were female, and 40.8% were black (Table 1). In addition, slightly more than half had self-reported hypertension, and nearly half of those with hypertension were uncontrolled.

Table 2 shows the prevalence of antihypertensive use over time. At baseline, over half reported the use of one or more antihypertensives, with calcium channel blockers being the most common class used (23%). At baseline, hydrochlorothiazide was the most common thiazide diuretic reported (94%). Also at baseline, 13.2% took a potassium sparing diuretic. The majority (93%) of potassium sparing diuretic use was with amiloride and triamterene, which are both epithelial sodium channel inhibitors (ENaC). ENaC use was almost always in combination with a thiazide diuretic (97%).

At baseline, the overwhelming majority reported taking an antihypertensive for more than 2 years and in doses ≤2 SDDs. By Year 6, 70% took one or more antihypertensives, with calcium channel blockers persisting as the most common class used (25.6%).

At baseline, 21.2% of participants reported any fall in the previous year. At year 2, 8% of participants reported having recurrent falls in the previous year. This rate remained somewhat stable over the next four waves (7.5%–10.4%; Table 3).

Table 4 shows the results from the multivariable model, controlling for demographic, health behavior/status, and access to care factors. While any antihypertensive use was found to increase the risk of recurrent falls in bivariate anlyses (crude odds ratio [OR] 1.89, 95% confidence interval [CI] 1.61–2.21), after controlling for a number of variables, we found that the adjusted odds ratio was reduced and no long showed a statistically significant increase in risk of recurrent falls (adjusted OR 1.13, 95% CI 0.88–1.46). Covariates with AOR > 1.0 and $p < .05$ were use of non-antihypertensive drugs that may increase risk of falls, arthritis, pulmonary disease, poor vision to completely blind, alcohol use, cerebrovascular disease, and diabetes. Similar findings were seen in those taking higher SDDs or for longer durations.

Of the eight subclasses, only loop diuretics were found associated with recurrent falls (adjusted OR 1.50, 95% CI 1.11–2.03). Post hoc analyses revealed no significant dose-response relationship among loop diuretic users (SDD ≥ 1, adjusted OR 1.53, 95% CI 0.88–2.65; SDD < 1, adjusted OR 1.53, 95% CI 1.08–2.15). However, those taking a loop diuretic for ≥2 years had a significant increase in risk, but not for a shorter period of time (adjusted OR 1.64, 95% CI 1.10–2.45 and adjusted OR 1.38, 95% CI 0.94–2.03, respectively). Post hoc analyses were also conducted in which three variables were created to capture the use of thiazide and potassium diuretics alone or in combination. They revealed that thiazide diuretic use only (adjusted OR 1.05), potassium-sparing diuretic use only (adjusted OR 0.92), or both diuretic types (adjusted OR 1.12) did not have a statistically significant (all $p > .05$) increased risk of recurrent falls.

Sensitivity analyses showed similar results when the sample was restricted to those with hypertension and stratified by blood pressure control (Supplementary Table 1). Similar results were also seen when the sample was stratified by those with a previous falls history at baseline (Supplementary Table 2). Multivariable analyses stratified by the median gait speed at baseline (1.17 m/s) found that any antihypertensive use did not increase the risk of recurrent falls in those with slower or faster gait speeds (AOR [95%CI] 0.61 [0.35–1.06] and AOR [95%CI] 0.99 [0.56–1.74]), respectively.

Discussion

This study assessed the association between antihypertensive use and recurrent falls in well functioning (at baseline) community-dwelling older adults. We found a nonsignificant 13% increase in risk of recurrent falls with any antihypertensive use. This is consistent with the non-significant findings from three other studies of antihypertensive drugs and recurrent falls in community dwelling elders (8–10).

This study also explored both dose– and duration–response relationships with any antihypertensive use and recurrent falls and found no increased risk. It is important to note our findings are robust in that our sensitivity analyses designed to address potential confounding by prior fall history and indication by restricting the sample to only those with hypertension revealed similar results.

In examining whether recurrent falls risk was elevated with use of any of seven antihypertensive subclasses, we found a statistically significant 54% increase in risk of recurrent falls associated with

Table 1. Characteristics of the Sample at Baseline (n = 2,948)

Variables	Antihypertensive User (n = 1,677), Mean ± *SD* or *N*, %	Not an Antihypertensive User (n = 1,271), Mean ± *SD* or *N*, %
Demographics		
Female gender	888 (53.0)	634 (50.0)
Black race	766 (45.7)	437 (34.4)
Site (Pittsburgh)	829 (49.4)	637 (50.1)
Age	73.6 (2.9)	73.6 (2.8)
Education		
Postsecondary	694 (41.4)	566 (44.5)
High school graduate	557 (33.2)	397 (31.2)
<High school	423 (25.2)	304 (24.0)
Married	857 (51.1)	674 (53.0)
Health behaviors		
Current smoker	153 (9.1)	149 (11.7)
Alcohol use (≥1 drink per week)	441 (26.3)	406 (31.9)
Health status		
Pulmonary disease	183 (10.9)	115 (9.0)
Arthritis	1,006 (60.0)	644 (50.7)
Urinary problems	305 (18.2)	190 (14.9)
Cerebrovascular disease	173 (10.3)	58 (4.6)
Bodily pain (any in past 30 d)	1,152 (68.7)	790 (62.2)
Vision problems		
Excellent/good sight	1,314 (78.4)	1,032 (81.2)
Fair sight	314 (18.7)	205 (16.1)
Poor to completely blind	47 (2.8)	34 (2.7)
Body mass index		
Underweight/normal (<24.9)	458 (27.3)	489 (38.5)
Overweight (25.0–29.9)	711 (42.4)	546 (43.0)
Obese (30+)	508 (30.3)	236 (18.6)
Excellent/very good/good self-rated health	1,328 (79.2)	1,151 (90.6)
Depressive symptoms (Short CES-D ≥ 10)*	108 (6.4)	60 (4.7)
Cognitive impairment (3MS < 80)*	162 (9.7)	122 (9.6)
Drugs that increase risk of falls* (benzodiazepines antidepressants, antipsychotics, opioids)	246 (14.7)	121 (9.5)
No. prescription medications*,†	2.1 (2.1)	1.3 (1.8)
Conditions where antihypertensives are indicated		
Self-reported hypertension*		
Controlled < 140/90 mmHg	695 (41.4)	80 (6.3)
Uncontrolled ≥140/90 mmHg	625 (37.3)	98 (7.7)
Peripheral arterial disease	112 (6.7)	37 (2.9)
Benign prostatic hyperplasia	413 (24.6)	279 (22.0)
Coronary heart disease	491 (29.3)	140 (11.0)
Congestive heart failure	77 (4.6)	8 (0.6)
Diabetes	322 (19.2)	118 (9.3)
Access to care		
Hospitalization in previous 12 mo	307 (18.3)	128 (10.1)
Private physician	1,352 (80.6)	967 (76.1)
Prescription insurance	1,109 (66.1)	752 (59.2)
Flu shot in previous 12 mo	1,225 (73.0)	814 (64.0)

Notes: 3MS = modified mini-mental status exam; CES-D = Center for Epidemiologic Studies Depression Scale; CNS = central nervous system; *SD* = standard deviation.

*Time varying.

†Excluding drugs that increase falls and antihypertensives.

loop diuretic use, but not with the remaining six. A small, case–control study similarly found over a twofold increase in risk of falling in loop diuretic users versus the comparison group (31.1% vs 13.3%; p < .05) (26). A nursing home study using a novel case-crossover design reported that nine persons with a loop diuretic change had a nearly 2.5-fold increased risk of a fall (27). Few other studies have found this relationship, however. A prospective cohort study of women found no association between loop diuretic use and recurrent falls (28). One explanation for the different findings may relate to duration of use, which we found to be an important factor. Further study is needed on the risk of falls with long-term loop diuretic use. One plausible explanation for this potential association is that loop diuretics can cause dehydration and/or orthostatic hypotension, potentially causing presyncope and leading to a fall.

Table 2. Antihypertensive Use OverTime*

Antihypertensive Medication Use	Year 1 (*n* = 2,948), *N* (%)	Year 2 (*n* = 2,811), *N* (%)	Year 3 (*n* = 2,679), *N* (%)	Year 5 (*n* = 2,489), *N* (%)	Year 6 (*n* = 2,388), *N* (%)
Any use	1,677 (56.9)	1,636 (58.2)	1,622 (60.5)	1,676 (67.3)	1,673 (70.1)
Long term (≥2 y) for any use	1,143/1,677 (68.2)	1,084/1,636 (66.3)	1,073 (66.2)	1,153/1,676 (68.8)	1,059/1,673 (63.3)
SDD ≥ 2	283 (9.6)	289 (10.3)	253 (9.4)	300 (12.4)	305 (12.8)
SDD = 1–2	546 (18.5)	555 (19.7)	584 (21.8)	668 (26.8)	662 (27.7)
SDD < 1	820 (28.7)	774 (28.1)	770 (29.3)	703 (28.4)	695 (29.6)
Specific class use	—	—	—	—	—
Beta blockers	395 (13.4)	409 (14.5)	434 (16.2)	520 (20.9)	572 (24.0)
Alpha blockers	364 (12.4)	317 (11.3)	284 (10.6)	264 (10.6)	238 (10.0)
Loop diuretics	178 (6.0)	195 (6.9)	207 (7.7)	263 (10.6)	265 (11.1)
Thiazide diuretics	582 (19.7)	593 (21.1)	557 (20.8)	599 (24.1)	579 (24.3)
Calcium channel blockers	678 (23.0)	662 (23.6)	642 (24.0)	631 (25.4)	611 (25.6)
ACE inhibitors	443 (15.0)	458 (16.3)	479 (17.9)	586 (23.5)	606 (25.4)
ARB	69 (2.3)	95 (3.4)	142 (5.3)	205 (8.2)	249 (10.4)
Vasodilators	35 (1.2)	20 (0.7)	18 (0.7)	9 (0.4)	10 (0.4)

Notes: ACE = angiotensin converting enzyme; ARB = angiotensin II receptor blocker; SDD = standardized daily dose of antihypertensives.
*No medication data were collected at Year 4 in the Health ABC Study.

Table 3. Prevalence of Recurrent and Single Falls OverTime

Variables	Year 2 (*n* = 2,948) *n*, %	Year 3 (*n* = 2,811) *n*, %	Year 4 (*n* = 2,679) *n*, %	Year 6 (*n* = 2,489) *n*, %	Year 7 (*n* = 2,388) *n*, %
2+ falls (recurrent)	240 (8.1)	210 (7.5)	229 (8.6)	259 (10.4)	206 (8.6)
1 fall	456 (15.5)	391 (13.9)	430 (16.1)	396 (15.9)	369 (15.5)

Table 4. Association Between Antihypertensive Use and Recurrent Falls Controlling for Covariates

Antihypertensive Medication Use*	Unadjusted OR (95% CI)	Adj. OR (95% CI)†
Any use	1.89 (1.61–2.21)	1.13 (0.88–1.46)
Long duration (≥2 y)	1.89 (1.60–2.24)	1.15 (0.88–1.49)
Short duration	1.89 (1.57–2.28)	1.11 (0.83–1.49)
SDD ≥2	2.12 (1.69–2.69)	1.21 (0.82–1.78)
SDD 1–2	1.93 (1.61–2.31)	1.05 (0.78–1.42)
SDD <1	1.79 (1.48–2.16)	1.16 (0.88–1.52)
Specific class use‡		
Beta blockers	1.22 (1.01–1.46)	1.06 (0.82–1.36)
Alpha blockers	1.29 (1.03–1.63)	1.25 (0.94–1.67)
Loop diuretics	1.60 (1.27–2.01)	1.50 (1.11–2.03)
Thiazide diuretics	0.97 (0.82–1.15)	0.87 (0.68–1.10)
Calcium channel blockers	1.23 (1.04–1.45)	1.06 (0.84–1.33)
ACE inhibitors	1.22 (1.01–1.47)	1.10 (0.85–1.42)
ARBs	1.35 (1.03–1.76)	1.17 (0.80–1.71)

Notes: ACE = angiotensin converting enzyme; adj = adjusted; ARB = angiotensin II receptor blocker; CI = confidence interval; OR = odds ratio.
*Reference group is no use.
†Controlling for variables forced into the model (ie, site, heart failure, BPH, cognitive impairment, depressive symptoms, self-reported hypertension [controlled/uncontrolled], drugs that increase risk of falls) and those from forward selection procedures (ie, education, age, marital status, alcohol use, cerebrovascular disease, diabetes, pulmonary disease, arthritis, urinary problems, vision problems, total number of prescription medications, syncope).
‡Each antihypertensive subclass was run as a separate model and controlled for antihypertensive subclass use other than the subclass being evaluated.

So what are some of the clinical implications of our findings? First, clinicians should feel comfortable prescribing chronically antihypertensives for the treatment of hypertension in older adults as recommended by recent guidelines and without fear that the risk of recurrent falls is increased (1). This is important since the use of these drugs results in a reduction of adverse cardiovascular events in patients ≥80 years of age. That said, rarely the initiation of some antihypertensives in high doses may cause orthostatic hypotension and syncope that could result in a serious fall (29–31). Because of this, the 2012 American Geriatric Society Beers Criteria suggest that the use of both peripheral and central alpha-blockers for hypertension be avoided in older adults (32). Clinicians should also consider

not prescribing loop diuretics for hypertension because there may be an increased risk of recurrent falls as documented by the current study. Moreover, some evidence suggests that thiazide diuretics are more effective in reducing elevated blood pressure than loop diuretics (33).

There are important potential limitations to our study. First, potential misclassification of the main outcome of recurrent falls has to be considered as it was retrospectively collected via self-report. However, it is a highly specific method in comparison to self-reporting of falls via diary (18). Moreover, there are limitations to the timing of the collection of falls data across the years that may have prevented some participants from being classified as a recurrent faller. In this respect, our recurrent fall rates are probably slight under estimates of the true rates. Second, medication data were collected at fixed annual assessments, preventing us from documenting the exact date in which antihypertensive medications were initiated, changed, or discontinued. Third, while it is possible that there is residual confounding, we were mindful of potential confounding bias and adjusted for common indications for antihypertensive therapy. Moreover, our sensitivity analyses showed similar results when restricted to only those with hypertension and when stratified by those with a baseline falls history. Fourth, we did not have information about the time of onset of hypertension. Fifth, because the majority of ENaC users were also taking a thiazide diuretic, it is difficult to say with confidence what the independent effect of their use was and thus it was not examined separately from the other seven antihypertensive classes. Sixth, we were unable to assess total duration of antihypertensive treatment. Finally, our analysis focused on older, well-functioning community-dwelling black and white men and women from the Memphis and Pittsburgh areas, and the generalizability to older adults in other regions or different care settings is unknown.

In conclusion, antihypertensive use overall was not statistically significantly associated with recurrent falls after adjusting for important confounders. Analyzed separately, however, loop diuretics were significantly associated with recurrent falls. Future research is needed with larger sample sizes in both community and long-term care facility settings with older adults to improve the evidence base on about medication-related fall risk.

Supplementary Material

Supplementary material can be found at: http://biomedgerontology.oxfordjournals.org/

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