

The Association between Antihypertensive Drugs and Falls in Older Adults in Amirkola, Northern Iran

M. Kamali (MD)¹, S. R. Hosseini (MD)^{*2}, R. Ghadimi (MD, PhD)², A. Rahimi (PhD)³,
A. Bijani (MD, PhD)²

1.Student Research Committee, Babol University of Medical Sciences, Babol, I.R.Iran.

2.Social Determinants of Health Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, I.R.Iran.

3.Cellular and Molecular Biology Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, I.R.Iran.

Article Type	ABSTRACT
Research Paper	Background and Objective: Being familiar with the factors that are effective in causing falls plays an important role in reducing the issues and costs related to its treatment. Considering the contradictory results about the use of antihypertensive drugs and falls in older adults, the present study was conducted to determine the association between the use of antihypertensive drugs and falls in older adults. Methods: This cross-sectional study was a part of the first phase of Amirkola Health and Ageing Project (AHAP), which was conducted on three groups of 250 people including healthy elderly, and hypertensive patients with and without taking antihypertensive drugs. Antihypertensive drugs were divided into 6 groups based on the mechanism of action. The variables of age, gender, body mass index, physical activity, diabetes, number of medications, depression symptoms, cognitive status, number of comorbidities, and the frequency of falls during one year before the beginning of the study and during the six-month follow-up were evaluated and compared in different categories of antihypertensive drugs by asking older adults in the three groups. Findings: Out of all studied older adults, 126 people (16.8%) fell during the last 12 months and 36 people (4.8%) fell during the six-month follow-up. No significant relationship was found between falls and the use of antihypertensive drugs, and between the use of different classes of antihypertensive drugs and falls. Variables such as depressive symptoms (OR=2.057, p=0.001), number of comorbidities (OR=0.189, p=0.006) and older age (OR=1.033, p=0.040) had an effective role in causing falls. Conclusion: The results of the study showed that the use of antihypertensive drugs and their different classes was not associated with the increase in the frequency of falls in older adults. Keywords: <i>Falls, Antihypertensive Agents, Risk Factors, Older Adults.</i>

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***Corresponding Author: S. R. Hosseini (MD)**

Address: Social Determinants of Health Research Center, Health Research Institute, Babol University of Medical Sciences, Babol, I.R.Iran.

Tel: +98 (11) 32190560. **E-mail:** hosseinirezaseyed@gmail.com

Introduction

Blood pressure is an important risk factor for cardiovascular diseases and its control plays an important role in reducing mortality from cardiovascular diseases (1, 2). In contrast to the benefits of antihypertensive treatment, there are also concerns about its side effects, including hypotension, falls, and fractures (3). Antihypertensive drugs cause falls by various mechanisms, including neurological and physical disturbances associated with electrolyte disturbances (4). On the other hand, some studies have stated that antihypertensive drugs reduce falls by improving brain blood flow (5). According to the definition of the World Health Organization, falls mean unintentionally falling on the ground or other lower surfaces (6). Falls are a serious problem in the elderly, and on average, 30% of the elderly fall every year (7). 1 in 5 cases of falls lead to serious injuries such as broken bones and brain damage (8). The risk factors of falls in the elderly are depression, movement limitation, low body mass index, history of falls in the past, and cognitive disorders (9).

Several studies are being conducted around the world regarding the use of antihypertensive drugs and falls in the elderly. In some of these studies, the use of antihypertensive drugs does not play a role in causing falls or being associated with a reduction in falls (10, 11). In a study by Margolis et al., the risk of falls was lower in women on long-term antihypertensive medication compared to those with normal blood pressure (12). On the other hand, there are studies that show that the use of antihypertensive drugs is associated with an increase in falls (13-16). In a study conducted by Richardson et al., the use of antihypertensive drugs was associated with an increase in falls (14).

Given the conflicting results of various studies, the aim of this study is to determine the relationship between the use of antihypertensive drugs and falls in older adults.

Methods

This cross-sectional study was approved by the Ethics Committee of Babol University of Medical Sciences with the code IR.MUBABOL.HRI.REC.1398.260 and is a part of the Amirkola Health and Ageing Project (AHAP) cohort study in 2011 and 2012 with the participation of 1616 elderly people (17). Follow-up of the project was done by phone and 6 months later by asking elderly people about falls and completing basic information.

The number of samples based on 95% confidence interval and 80% power and assuming $p=20\%$ and $p=10\%$ regarding the frequency of falls in the groups with and without the use of antihypertensive drugs, 196 people were estimated in each group and to increase the power of the study, 250 samples were included in each group. In this study, elderly people with high blood pressure with and without taking antihypertensive drugs were selected as the case group and non-hypertensive people were selected as the control group. People with high blood pressure who did not take medication were those who did not know about their disease status and found out about their disease in the elderly cohort study. The status of falls during the last 12 months was determined and investigated in all three groups at the beginning of the study and once again after 6 months of follow-up. People with severe cognitive impairment with a Mini Mental State Examination (MMSE) score less than or equal to 9 and severe balance impairment with a score less than 20 and inability to answer questions were excluded from the study (18). In this study, the meaning of falls is the fall of an elderly person on the same level or higher and shorter levels, in such a way that it leads to physical damage in the elderly person and may or may not require treatment (6).

Data about falls were collected by asking the elderly person or his/her companion. The falls questionnaire includes the history of falls in the initial examination as well as the six-month follow-up. In this study, high blood pressure was diagnosed based on blood pressure measurement using the Omron M3 Intelligence sphygmomanometer in supine position on two occasions in a standard way. High blood pressure in this study was defined as mean SBP ≥ 140 mmHg or DBP ≥ 90 mmHg. Also, if there is a difference of 20 mm Hg or more in systolic blood pressure and 10 mm Hg or more in diastolic blood pressure in both supine and standing positions, it was considered as postural hypertension disorder (19). Data on the use of antihypertensive drugs were collected by asking the patient or his/her companions and by observing the drugs used and the doctor's prescription. Antihypertensive drugs used in the elderly were classified into Diuretics, Beta-blockers, ACE inhibitors, Angiotensin II receptor blockers, Calcium channel blockers and Alpha-blockers. All demographic information such as age, gender, height and weight, education, occupation and smoking were recorded in all the elderly in the case and control groups. Diagnosing diabetes was done based on World Health Organization criteria and by measuring fasting blood sugar (FBS ≥ 126 mg/dl) in two sessions (20).

Chronic diseases in this study included diabetes, hyperthyroidism and hypothyroidism, stroke, Parkinson's, dementia, depression, epilepsy, heart attack and angina pectoris, heart failure, asthma and emphysema, liver disease, kidney disease, kidney stones, stomach ulcer, urinary incontinence, fecal incontinence, any type of cancer, headache, arthritis, hearing loss, and fractures, all of which were self-reported. Furthermore, the diagnosis of other chronic diseases such as diabetes, high blood pressure, cognitive impairment and depression was based on examinations and tests.

To evaluate the cognitive status, the Brief Mental Status Evaluation Questionnaire (MMSE) was used (18). A score of 22 was considered as the cutoff point. In this score, the test has a sensitivity of 90% and a specificity of 93.5%. Its validity and reliability have been confirmed in the Iranian population (21). Using a 15-question standard questionnaire (Geriatric Depression Scale= GDS), the presence of depression symptoms in the elderly was investigated. A score of 0 to 4 is normal, 5 to 8 is classified as mild depression, a score of 9 to 11 is classified as moderate depression, and a score of 12 to 15 is classified as severe depression (22). In Iran, Malakouti et al. reported the alpha coefficient and its reliability as 0.96 and 0.85, respectively (23).

The physical activity of the elderly was collected using the Physical Activity Scale for Elderly (PASE) questionnaire. This questionnaire includes three sections: leisure time, home activity and work activity. The score of this questionnaire is 0-400, and a higher score indicates a higher level of activity (24). The validity and reliability of this questionnaire in Farsi has been investigated (25). Quadriceps muscle strength was calculated using a dial scale, and the maximum force that the patient applied to the spring gauge was recorded in kilograms separately for the right and left leg. Hand muscle strength was measured using a Digi hand dynamometer (Korea). People were asked to make a fist with their maximum strength and press the dynamometer, and the maximum force that was applied was considered as the strength of the hand muscles in kilograms.

Berg Balance Test (BBT) was used to measure balance in the elderly. People who scored between 41-56 were in the group of normal balance and people with a score of less than 20 were in the group at high risk of falls (26). After measuring height and weight, body mass index (BMI) was calculated and people with BMI less than 18.5 were considered underweight, 18.5-24.9 normal and BMI ≥ 25 as overweight and fat. The obtained data were entered into SPSS 18 software and analyzed using descriptive and analytical statistical tests such as chi-square test to compare qualitative variables and ANOVA test to compare continuous and quantitative data. Furthermore, the multiple logistic regression model was used to determine the role of variables affecting falls in the elderly. In all cases, $p < 0.05$ was considered significant.

Results

Out of a total of 750 elderly people examined, 50% of them were women and 644 (85.9%) of them were married. In terms of education level, 429 people (62.5%) were illiterate and 59 people (7.9%) had high school diploma and university education. Moreover, out of all the people examined, 134 people (17.9%) smoked cigarettes. In this study, 63.2% of healthy people, 52.8% of people with high blood pressure who were not taking medication, and 51.2% of people with high blood pressure who were taking medication had postural hypotension, and this difference was statistically significant ($p=0.014$). Furthermore, the prevalence of diabetes in healthy people, people with high blood pressure with and without medication was 20.8%, 42.8% and 31.6%, respectively ($p=0.000$) (Table 1).

Table 1. Frequency distribution and percentage of basic information in the elderly of Amirkola

Variable	Group	No hypertension Number(%)	Hypertensive without medication Number(%)	Hypertensive with medication Number(%)	p-value
Education level					
	Illiterate	151(60.4)	173(69.2)	145(58)	0.053
	Elementary	82(32.8)	61(24.4)	79(31.6)	
	High school and university	17(6.8)	16(6.4)	26(10.4)	
Smoking					
	Yes	49(19.6)	41(16.4)	44(17.6)	0.641
	No	201(80.4)	209(83.6)	206(82.4)	
Marital status					
	Married	218(87.2)	217(86.8)	209(83.6)	0.488
	Single	32(12.8)	33(13.2)	41(16.4)	
Physical activity					
	Suitable	69(27.6)	51(20.4)	51(20.4)	0.086
	Unsuitable	181(72.4)	199(79.6)	199(79.6)	
Diabetes					
	Yes	52(20.8)	79(31.6)	107(42.8)	0.000
	No	198(79.2)	171(68.4)	143(57.2)	
Postural hypotension					
	Yes	158(63.2)	132(52.8)	128(51.2)	0.014
	No	92(36.8)	118(47.2)	122(48.8)	

The average number of concomitant diseases and the number of drugs consumed and the body mass index in the three groups showed statistically significant differences; the average value of all three variables was significantly higher in the group that had high blood pressure and was taking drugs ($p=0.000$). The average heart rate and systolic and diastolic blood pressure in the standing and lying positions were also higher in the group that had high blood pressure and did not take medication ($p=0.000$). The average results of the short test of mental status, depression state, physical activity score, arm and quadriceps muscle strength were similar in three groups of elderly people (Table 2).

Table 2. The average of the investigated variables in the studied groups in the elderly of Amirkola

Variable	Group	No hypertension Mean±SD	Hypertensive without medication Mean±SD	Hypertensive with medication Mean±SD	p-value
Age (years)		67.68±6.71	67.96±6.64	67.62±6.42	0.826
Supine Heart Rate		72.25±11.02	74.79±11.77	70.70±11.84	0.000
Systolic blood pressure in supine position (mmHg)		126.10±11.20	154.43±17.55	150.03±22.52	0.000
Diastolic blood pressure in the supine position (mmHg)		75.12±8.34	87.33±10.12	84.38±12.56	0.000
Standing heart rate		83.62±13.73	83.03±13.07	77.93±13.63	0.000
Standing systolic blood pressure (mmHg)		121.07±14.54	147.39±21.28	141.40±25.01	0.000
Standing diastolic blood pressure (mmHg)		78.18±9.48	88.35±11.45	86.06±13.61	0.000
Short mental state test score		25.52±3.23	25.15±3.48	25.82±3.24	0.790
Depression questionnaire score for the elderly		4.20±3.60	4.33±3.30	4.75±3.40	0.180
Number of chronic diseases		1.95±1.64	2.58±2.07	3.67±1.72	0.000
Physical activity score		117.86±56.88	108.38±60.94	108.39±62.28	0.126
Number of drugs		1.18±1.72	1.27±1.85	4.69±2.38	0.000
body mass index (kg/m ²)		26.30±4.60	27.87±4.60	28.10±4.15	0.000
Arm muscle strength (kg)		25.81±9.23	26.22±10.31	28.29±20.63	0.117
Quadriceps strength (kg)		22.59±10.00	23.13±11.20	22.14±10.16	0.573

The frequency of falls during the last 12 months was higher in the group with high blood pressure and taking antihypertensive drugs than the other groups, although this difference was not statistically significant. Moreover, during the 6-month follow-up, there was no significant difference in the frequency of falls in the three groups (Table 3).

In this study, during the last 12 months, ARB class with 25% and beta blocker with 20% had the highest percentage of falls compared to other classes of antihypertensives. Diuretic also had the lowest percentage of falls with 12.2%, although it was not statistically significant. Moreover, the frequency of falls during the 6-month follow-up was not significantly different in any of the antihypertensive drug categories.

Table 3. Distribution of frequency and percentage of falls in the groups under study in the last 12 months and 6-month follow-up in the elderly of Amirkola

Falls	Group	No hypertension Number(%)	Hypertensive without medication Number(%)	Hypertensive with medication Number(%)	p-value
Falls over the past 12 months					
Yes		36(14.4)	41(16.4)	49(19.6)	0.292
No		214(85.6)	209(83.6)	201(80.4)	
Fall during 6-month follow-up					
Yes		13(5.2)	11(4.4)	12(4.8)	0.916
No		237(94.8)	239(95.6)	238(95.2)	

Logistic regression model was used to investigate the role of influencing variables in causing falls. The variables of having depressive symptoms ($p=0.001$, 95% CI=1.329-3.182, OR=2.057) the number of concomitant diseases ($p=0.006$, 95% CI=1.051-1.346, OR=1.189) and age ($p=0.040$, 95% CI=1.002-1.065, OR=1.033), respectively, had the greatest role in causing falls. Having or not having high blood pressure and taking or not taking antihypertensive drugs had no effect on causing falls (Table 4).

Multivariable logistic regression model was used to determine the role of antihypertensive drug categories in causing falls. In this analysis, none of the classes of antihypertensive drugs had a significant role in causing falls in the elderly. Also, in this study, the simultaneous consumption of 2 drug categories and also some combinations including 3 drug categories at the same time did not have a significant role in causing falls.

The frequency and percentage of falls in all three groups were higher in women and in people who used antihypertensive drugs (Figure 1).

Table 4. Multivariate analysis of risk factors of falls using logistic regression

Variable	Odds Ratio (OR)	Confidence (CI 95%)Interval	p-value
Group			
Normal people	1	-	-
Hypertensive without medication	1.053	0.262-1.771	0.845
Hypertensive with medication	1.065	0.583-1.944	0.839
Diabetes	0.926	0.590-1.462	0.751
Number of drugs	1.007	0.907-1.118	0.895
Orthostatic hypotension	1.102	0.731-1.663	0.642
Physical activity	0.889	0.540-1.497	0.683
MMSE score	0.979	0.623-1.540	0.928
Body mass index			
20-24.99	1	-	-
25-29.99	0.937	0.580-1.514	0.791
≥ 30	0.744	0.419-1.323	0.314
Number of comorbidities	1.189	1.051-1.346	0.006
Symptoms of depression	2.057	1.329-3.182	0.001
Age	1.033	1.002-1.065	0.040
Gender (female to male ratio)	1.303	0.818-2.077	0.265

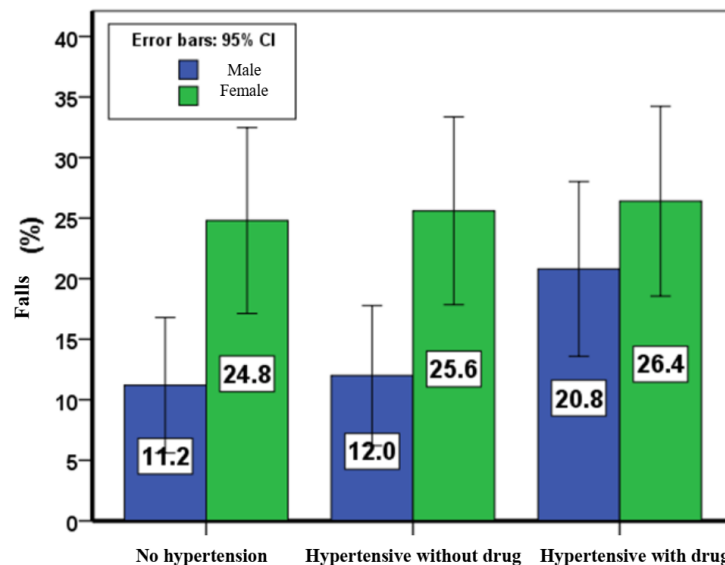


Figure 1. The frequency of falls in the studied groups according to gender in the elderly of Amirkola

Discussion

In this study, there was no significant relationship between falls and the use of antihypertensive drugs in the elderly. Although the frequency of falls in people with high blood pressure who took antihypertensive drugs was higher than the other groups, which was similar to the results of the studies of Kjellberg et al., Juraschek et al., and Na'emani et al., in which no relationship was found between the use of antihypertensive drugs and falls (11, 27, 28), the results of studies by Tinetti et al., Richardson et al., Ren et al., and Ye et al. showed that the use of antihypertensive drugs was associated with an increased risk of falls (13-16). The reason for this difference could be the higher mean age (81 years) and the use of more drugs (an average of 7 drugs) in the study by Richardson et al. (14). In addition, the larger number of samples (9692 people) in the study of Ren et al. (15), longer follow-up (one year) and larger sample size (265,225 people) in the study of Ye et al. (16) might have caused this difference with the results of the present study.

Other results of the present study showed that chronic diseases, depression symptoms, history of falls in the last 12 months and older age were associated with falls. On the other hand, it was found in this study that the variables of gender, education level, body mass index, diabetes, physical activity, orthostatic hypotension, the number of drugs used, and MMSE are not related to falls.

Unlike the present study, in the study of Tinetti et al., the factors of older age, gender, diabetes and smoking were associated with a higher risk of falls. Moreover, the presence of depressive symptoms and a history of falls in the past were associated with more falls, which is similar to the results of the present study (13).

In the study of Lipsitz et al., depressive symptoms and the number of chronic diseases were associated with an increased risk of falls, which is consistent with the results of the present study. It was also found that higher education level and cognitive impairment and diabetes increase the risk of falls, which was not consistent with the results of our study. Although in our study, people with severe cognitive impairment were excluded from the study (29).

Similar to our study, according to the study of Margolis et al., people who had more chronic diseases, history of previous falls, and older age, experienced more falls. Moreover, people with higher education level and lower BMI experienced more falls, which was not consistent with our study (12).

In the study of Wong et al., it was found that older age and depressive symptoms were not related to falls, while in our study, these two variables were associated with more falls. On the other hand, similar to our study, gender, BMI, MMSE, and orthostatic hypotension were not associated with falls in the study of Wong et al. It was also found that the history of falls in the past year was associated with more falls, which is similar to the present study (7).

Another result of this study was the lack of correlation between different classes of blood pressure medications and the simultaneous use of two or three classes in reducing or increasing the risk of falls. In the study of Tinetti et al., it was found that none of the classes of antihypertensive drugs were associated with an increase in falls, which was consistent with our study (13).

However, in the study of Lipsitz et al., CCB and ACEI classes were associated with a reduction in the risk of falls, which is not consistent with the results of our study. It was also found that beta-blocker, alpha-blocker, diuretic, and ARB classes were not associated with a decrease or increase in the risk of falls, which was similar to our study (29).

In the study of Margolis et al., it was found that beta blockers increase the risk of falls and diuretics decrease the risk of falls, which was not consistent with our study. Furthermore, alpha blocker, ACEI, ARB, and CCB were not associated with decreasing or increasing the risk of falls, which was similar to our study (12). Unlike the present study, in the study of Wong et al., it was found that the use of diuretics was associated with an increased risk of falls and the use of ARB alone or in combination with ACEI was

associated with a reduced risk of falls (7). In addition, in the study of Shea et al., the use of ACEI and ARB drugs was associated with a reduction in the risk of falls (10). In the study of Banu et al., it was found that the use of a class of antihypertensive drugs was not associated with an increase in falls, which was similar to our study. It was also found that the use of two or more classes of antihypertensive drugs increased falls, which was contrary to our study (30).

One of the strengths of our study is the presence of extensive data, including demographic information, medications used, and accurate data measurement. Moreover, the data of this study was based on the general population and with a relatively large sample size, which was another strength of our study. The limitations of the current study include the cross-sectional nature of the study and the impossibility of examining the cause – and – effect relationship, the small number of users of some drug categories such as alpha blocker and CCB, lack of information such as the dosage, the time of starting the drug, changing the prescription during the 6-month follow-up, and the type of falls (minor or major). In addition, we could not identify the elderly people who did not report or underreported their falls. The insufficiency of the follow-up period and the few cases of falls during this period were other limitations that made it difficult to analyze the data according to drug classes.

The present study showed that the frequency of falls in hypertensive patients who took antihypertensive drugs was higher than in healthy individuals, but it was not statistically significant, although in this study it was not possible to investigate the cause – and – effect relationship and controlling all distractors was not possible. Moreover, no relationship was found between falls and the use of any of the classes of antihypertensive drugs and their number.

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