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A Multicenter, Case-Control Study of the Effects of Antihypertensive Therapy on Orthostatic Hypotension, Postprandial Hypotension, and Falls in Octo- and Nonagenarians in Residential Care Facilities

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ABSTRACT

Background: Orthostatic hypotension, postprandial hypotension, and falls are considered to be adverse drug reactions of antihypertensive therapy in older people with comorbidities. Concerns regarding these adverse events may limit the use of antihypertensive agents in this group of people.

Objective: The aim of this study was to determine the relationship between antihypertensive therapy in octo- and nonagenarians and the risk for orthostatic hypotension, postprandial hypotension, and falls.

Methods: This was a case-control study of octo- and nonagenarians living in residential care facilities who were receiving antihypertensive therapy and a control group who were not receiving antihypertensive therapy.

Results: A total of 119 patients, 77 who were receiving regular antihypertensive therapy and 42 who were not taking any antihypertensive agents, were enrolled in the study. The prevalence of antihypertensive use, orthostatic hypotension, postprandial hypotension, and falls was high (65%, 29%, 57%, and 45%, respectively). There were no associations between antihypertensive therapy and orthostatic hypotension, postprandial hypotension, and falls. When individual classes of antihypertensive agents were examined, the only observed association was a negative association (ie, a protective effect) between potassium-sparing diuretics and falls (odds ratio, 0.2; 95% CI, 0.04–1.0).

Conclusion: Antihypertensive therapy was not associated with an increased risk for orthostatic hypotension, postprandial hypotension, or falls in this

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case-control study of octo- and nonagenarians living in residential care facilities. (*Curr Ther Res Clin Exp.* 2003;64:206–214)

Key words: older people, antihypertensives, orthostatic hypotension, postprandial hypotension, falls.

INTRODUCTION

The benefits of antihypertensive therapy in 15 randomized clinical trials involving 21,908 older patients have been reviewed.[1,2] Most of these trials included patients aged 60 to 80 years and were used to assess beta-blockers and diuretics over a period of 3 to 6 years. The number of patients in this age group that need to be treated to prevent cardiovascular morbidity and mortality has been estimated to be 19 (95% CI, 14–32); the benefits also are seen for older patients with isolated systolic hypertension.[1,2] Data on the efficacy of antihypertensive treatment for patients aged >80 years and for frail elderly patients are limited.[3] The evidence base may be increased by clinical trials in very old (ie, aged >80 years) patients (eg, Hypertension in the Very Elderly Trial[3] and Swedish Trial in Old Patients with Hypertension-2[4] [STOP-2]). On the other hand, observational studies suggest that a positive relationship exists between blood pressure (BP) and survival, and the benefits of antihypertensive therapy seen in the Systolic Hypertension in the Elderly Program (SHEP), European Working Party on High Blood Pressure in the Elderly (EWPHE), and Systolic Hypertension in Europe (SYST-EUR) studies[5] were diminished in the oldest groups of elderly patients.

One of the major considerations when commencing any medications in geriatric patients, including antihypertensive drugs, is the high prevalence of adverse drug reactions. In older patients receiving antihypertensive therapies, potential adverse drug reactions of concern include orthostatic hypotension,[6–8] postprandial hypotension,[9] and falls.[8,10,11] This prevents some clinicians from prescribing antihypertensive agents to older people,[7,8] with 25% of clinicians believing that antihypertensive drugs are associated with more risks than benefits in this age group.[12]

Orthostatic hypotension occurs in 5% to 33% of older people and contributes to the risks of syncope and falls.[6] Medications frequently are considered to be a major cause of orthostatic hypotension in older people.[6] Postprandial hypotension has been less intensively investigated in older people than orthostatic hypertension; however, an association with antihypertensive therapy has been reported[9] and postprandial hypotension is a risk factor for falls.[13] Finally, the relationship between medications and falls is important in clinical geriatric practice.[14] Because falls are not defined as an adverse drug reaction in most clinical trials, most of the evidence linking falls to antihypertensive therapy has been obtained from observational studies. Many such studies have shown an association between falls and antihypertensive drugs[10]; however, a meta-analysis found less evidence for any association, except for diuretics.[15]

The decision to commence antihypertensive therapy in very old people is often influenced by concerns regarding these outcomes.[8]

The aim of this study was to determine the relationship between antihypertensive therapy in octo- and nonagenarians and the risk for orthostatic hypotension, postprandial hypotension, and falls. We chose to study older people in residential care facilities because they generally have more comorbidities and require complex pharmacotherapies. More importantly, data on falls are routinely collected in nursing notes, providing a useful record of the prevalence and frequency of falls.

PATIENTS AND METHODS

Patients aged >80 years residing in 8 residential care facilities were recruited as part of a larger case-control study of the relationship between postprandial hypotension and falls.[13] Subjects were in residential care because of high levels of disability, and the only subjects excluded from the study were those with cognitive impairment (Mini-Mental State Examination score ≤20 out of 30) that precluded informed consent. The study was approved by the Australian Capital Territory Health and Community Care Ethics Committee. All participants provided written informed consent.

Medical histories and data were confirmed using medical and nursing records, medication sheets, and hospital and general practitioner records. Patients fasted overnight and medications were withheld. BP and heart rate were obtained using an oscillometric cuff (Ambulatory Blood Pressure Monitor, Spacelabs Medical, Inc., Issaquah, Washington) calibrated against a mercury sphygmomanometer. The following BP measurements were taken: (1) lying, fasted; (2) after standing for 1 minute; (3) after standing for 3 minutes; (4) after sitting for 15 minutes before breakfast; and (5) sitting, 60 minutes after breakfast was completed. All measurements were performed twice on the same arm. Orthostatic hypotension was defined as a decrease in systolic BP of ≥20 mm Hg and/or in diastolic BP of ≥10 mm Hg within 3 minutes of standing. Postprandial hypotension was defined by the same criteria comparing BP measurements in the sitting position before and 60 minutes after breakfast. Postprandial BP measurements were taken 60 minutes after the meal because this is the time when BP is usually lowest. The meal challenge was the usual breakfast for maximum clinical relevance to the individual.

A *fall* was defined as a sudden, unintentional landing on the floor or ground with or without loss of consciousness or injury, other than as a consequence of the sudden onset of paralysis, an epileptic seizure, or overwhelming external force.

Statistical Analysis

Data are presented as means (SD). Univariate comparisons were performed using the odds ratio and chi-square test. $P < 0.05$ was considered statistically significant.

Table. The odds ratios (95% CI) for orthostatic hypotension, postprandial hypotension, and falls in all study patients (N = 119). Some patients were taking several antihypertensive medications.

Antihypertensive Medications	No. (%) of Patients	Orthostatic Hypotension	Postprandial Hypotension	Falls
All antihypertensives	77 (65)	0.8 (0.3–1.7)	0.9 (0.4–1.8)	0.8 (0.4–1.6)
All diuretics	39 (33)	0.6 (0.2–1.5)	0.8 (0.4–1.9)	0.6 (0.3–1.4)
ACEI	33 (28)	1.3 (0.5–3.1)	0.9 (0.4–1.9)	1.0 (0.5–2.3)
CCB	29 (24)	2.1 (0.9–4.9)	0.6 (0.3–1.4)	1.4 (0.6–3.2)
Beta-blocker	18 (15)	0.6 (0.2–2.1)	0.4 (0.2–1.2)	1.2 (0.5–3.4)
Thiazide	14 (12)	0.6 (0.2–2.4)	2.0 (0.6–6.9)	0.4 (0.1–1.5)
Potassium-sparing diuretic	12 (10)	0.8 (0.2–3.1)	1.6 (0.4–5.5)	0.2 (0.04–1.0)

ACEI = angiotensin-converting enzyme inhibitor; CCB = calcium channel blocker.

RESULTS

Patient Characteristics

One hundred nineteen patients (99 women, 20 men; mean [SD] age, 87 [4] years) were included in the study. The mean (SD) number of medical diagnoses per patient was 3.9 (1.9). The mean (SD) number of medications per patient was 5.8 (2.9); these included benzodiazepines (34%), digoxin (28%), nitrates (20%), selective serotonin reuptake inhibitors (12%), and tricyclic antidepressants (12%). Sixty-five percent of patients were taking at least 1 antihypertensive medication (Table). The age and sex of patients taking antihypertensive medications (n = 77) were similar to those of patients not taking antihypertensive medications (n = 42) (mean [SD] age, 87 [4] years vs 87 [3] years, respectively; 88% vs 73% women, respectively). The patients taking antihypertensive medications were more likely to report a history of ischemic heart disease (odds ratio [OR], 5.8; 95% CI, 2.2–15.5) and atrial fibrillation (OR, 3.8; 95% CI, 1.4–10.2); otherwise, no significant differences in comorbidities were found between groups.

On the basis of BP measurements, 26% of patients had stage 1 hypertension (systolic BP 140 to 159 mm Hg or diastolic BP 90 to 99 mm Hg), 20% had stage 2 hypertension (systolic BP 160 to 179 mm Hg or diastolic BP 100 to 109 mm Hg), and 29% had stage 3 hypertension (systolic BP ≥180 mm Hg or diastolic BP ≥110 mm Hg). Furthermore, 26% of patients had isolated systolic hypertension and 3% had isolated diastolic hypertension. Sixty-five percent of patients were taking at least 1 antihypertensive medication. BP was in the normal range in 15% of patients with treated hypertension and in 36% of patients who were not taking antihypertensive therapy. Mean (SD) BP in patients taking antihypertensive medications (160 [27]/83 [11] mm Hg) was not significantly different from mean BP in those not taking antihypertensive medications (158 [24]/83 [15] mm Hg).

Orthostatic Hypotension and Antihypertensive Therapy

The mean (SD) BP was 159 (26)/83 (15) mm Hg in the supine position and 152 (31)/84 (16) mm Hg after standing for 1 minute, with a mean (SD) decrease in BP of 8 (20)/1 (12) mm Hg. Orthostatic hypotension was present in 29% of patients. Antihypertensive therapy was not associated with an increased risk for orthostatic hypotension. BP decreased to 155 (33)/84 (16) mm Hg in those taking antihypertensive medications and to 146 (26)/85 (16) mm Hg in those not taking antihypertensive medications after standing for 1 minute.

Postprandial Hypotension and Antihypertensive Therapy

Before breakfast, the mean (SD) BP was 164 (28)/87 (15) mm Hg and decreased to 146 (26)/76 (14) mm Hg 60 minutes after eating, with a mean decrease in BP of 18 (21)/11 (13) mm Hg. Postprandial hypotension was present in 57% of patients. Antihypertensive therapy was not associated with an increased risk for postprandial hypotension. After a meal, mean BP decreased to 148 (27)/77 (15) mm Hg in patients taking antihypertensive medications and to 142 (22)/74 (11) mm Hg in those not taking antihypertensive medications.

Falls and Antihypertensive Therapy

Forty-five percent of patients had at least 1 fall in the past year, and 57% of these patients had recurrent falls. Falls were associated with fractures (33%), soft tissue injury (26%), and loss of consciousness (8%). Antihypertensive therapy was not associated with an increased risk for falls, and potassium-sparing diuretics had a protective effect (OR, 0.2; 95% CI, 0.04–1.0).

DISCUSSION

Although evidence of the benefits of antihypertensive therapy in the oldest and the most frail elderly patients is limited, extrapolation of the results of clinical trials in patients aged <80 years with limited comorbidities [1,2,4,5,8] suggest that such therapy is beneficial. Sixty-five percent of the patients in this study were taking at least 1 antihypertensive agent. Our patients were aged >80 years, required residential care because of disability, and had numerous comorbidities. These findings indicate a willingness by clinicians in this region to prescribe antihypertensive drugs to frail elderly people. Antihypertensive therapies prescribed included diuretics, angiotensin-converting enzyme inhibitors (ACEIs), and calcium channel blockers (CCBs), with beta-blockers prescribed less frequently. This is consistent with other reports and indicates that clinicians tend to prefer newer antihypertensive drugs (ACEIs and CCBs) to those usually recommended by guidelines (diuretics and beta-blockers).[16]

Although data specifically on very elderly people in residential care are limited, the prevalence of hypertension, orthostatic hypotension, postprandial hypotension, and falls observed in this study was similar to that reported in various other groups of older people. We found that 77% of the patients had a

high BP reading on the study day, 65% were taking at least 1 antihypertensive medication, and only 15% of these treated hypertensive patients had their BP controlled. Other reports have concluded that 60% to 70% of people aged >65 years have hypertension, although some of these do not have sustained hypertension[17] and only ~10% have their BP fully controlled.[18] We found that 29% and 57% of our patients had orthostatic and postprandial hypotension, respectively, which is similar to the findings in other studies.[13,19–21] Forty-five percent of our patients had a history of falls, which is also similar to other studies.[22,23]

We did not find any association between antihypertensive therapy and orthostatic hypotension, although BP readings were measured only ≥12 hours after medication administration on 1 occasion. In the past, the association between antihypertensive therapy and orthostatic hypotension in older patients was considered to be well established.[6] The newer agents used to treat hypertension may be less likely to produce orthostatic hypotension than the older agents, [7] although an association between orthostatic hypotension and CCBs and diuretics in patients aged >65 years was found in 1 study.[21] Effective management of hypertension, by delaying vascular dysfunction, may even protect against orthostatic hypotension. However, the lack of any association between antihypertensive therapy and orthostatic hypotension in our study may simply reflect the lack of aggressiveness of treatment, with only 15% of treated patients having their BP controlled.

We also did not find any association between antihypertensive therapy and postprandial hypotension. Some studies have shown an association between postprandial hypotension and diuretics[9]; vasodilators[24]; and ACEIs, CCBs, diuretics, nitrates, digoxin, and psychotropic drugs.[25] It has also been reported that antihypertensive therapy may reduce postprandial hypotension.[20,26–28]

Finally, we did not find any association between antihypertensive therapy and falls. The relationship between falls and drug therapy relies on observational studies such as this one because falls usually are not classified as an adverse drug reaction in clinical trials. The association between cardiovascular drugs and falls is controversial. Some studies have shown an association, with the mechanism often considered to be orthostatic hypotension.[29,30] However, orthostatic hypotension is more likely to produce syncope, which often is excluded from research-based definitions of falls. In a meta-analysis of 29 published studies, Leipzig et al[15] reported that the pooled odds ratios for falls were 1.20 (95% CI, 0.92–1.58) for ACEIs, 1.16 (95% CI, 0.87–1.55) for centrally acting antihypertensives, 1.08 (95% CI, 1.02–1.16) for diuretics, 1.06 (95% CI, 0.97–1.16) for thiazide diuretics, 0.94 (95% CI, 0.77–1.14) for CCBs, and 0.93 (95% CI, 0.77–1.11) for beta-blockers. We found a negative association (ie, a protective effect) between potassium-sparing diuretics and falls. Although this observation is limited by population size and multiple comparisons, on the basis of a MEDLINE search (1966 to 2002; search terms: *falls, medications, elderly*), this is the

first study in which a protective effect against falls has been observed with any medication.

This study of octo- and nonagenarians living in residential care facilities who have high levels of comorbidity and polypharmacy shows that antihypertensive therapy used in routine clinical practice is not associated with an increased risk for orthostatic hypotension, postprandial hypotension, or falls. This case-control, observational study was limited by various biases, including selection bias. In particular, prescribers may have withheld antihypertensive therapy in patients with a high risk for falls. On the other hand, few randomized clinical trials have been performed in very elderly patients with multiple comorbidities. Therefore, this methodology is appropriate; indeed, it is the only readily available methodology for the determination of the frequency of adverse drug reactions. Because older people have a high prevalence of adverse drug reactions, such evidence is crucial for making informed risk-benefit decisions about prescribing in frail, older people.

CONCLUSION

Antihypertensive therapy was not associated with an increased risk for orthostatic hypotension, postprandial hypotension, or falls in this case-control study of octo- and nonagenarians living in residential care facilities.

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