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Association between sleep characteristics and antihypertensive treatment in older adults

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Aim: The relationship between sleeping characteristics and antihypertensive medication is little known. We examined the association of sleep quality or duration and the use of sleeping pills with the number of antihypertensive drugs used in older adults.

Methods: This was a prospective cohort study of treated hypertensive patients aged ≥60 years participating in a seniors cohort, followed from 2008 to 2010 through 2012 to 2013. Self-reported sleep duration, sleep quality (usually having difficulty falling asleep or staying asleep) and sleeping pills use were ascertained at baseline, and the change in the number of antihypertensive drugs (active agents) between 2008–2010 and 2012–2013 was calculated. Analyses were carried out with logistic regression, and adjusted for demographics, lifestyle, comorbidity, baseline number of antihypertensive drugs and hypertension control.

Results: Among the 752 participants at baseline (mean age 69.9 years, 49.2% men), the mean sleep duration was 6.9 h/day, 37% had poor sleep quality, 16.5% usually consumed sleeping pills and the mean number of antihypertensive drugs was 1.8. During the follow-up period, 156 (20.7%) patients increased the number of antihypertensive drugs. No association was found between sleep duration or quality and the change in antihypertensive drug use. Usual sleeping pills consumption was associated with a higher risk of increasing (*vs* decreasing/maintaining) the number of antihypertensive drugs (odds ratio 1.85; 95% confidence interval 1.12–3.07, *P*-value 0.02).

Conclusions: Consumption of sleeping pills was prospectively linked to an increased number of antihypertensive drugs. "Sleeping pill use" might be an indicator of future needs of antihypertensive treatment, and a warning indicator to investigate underlying sleep disorders or unhealthy lifestyles. **Geriatr Gerontol Int 2019; ••: ••–••.**

Keywords: antihypertensive drugs, blood pressure, elderly, hypertension, sleep.

Introduction

Hypertension is very frequent in older people, who are thus at increased cardiovascular risk; nevertheless, antihypertensive treatment has generally shown to reduce such risk, although the blood pressure target in older patients is still debated.[1–3] Also, approximately 50% of older adults complain about difficulty with initiating or maintaining sleep.[4]

Many studies have generally found associations of sleep characteristics with blood pressure and hypertension in middle-aged adults,[5–10] however these associations were absent or inconsistent among older adults.[7,8,11,12] Furthermore, hypertensive patients might change their needs of antihypertensive drug treatment over time depending on the levels of blood pressure achieved.[13] Here again, sleep disorders might be at work; for example, one study reported that antihypertensive drug users were more likely to take sleep medications.[14] However, to our knowledge this association has not been further examined, in particular in older adults.

The present study examined whether sleeping characteristics (duration, quality and frequency of sleeping pills consumption) were associated with prospective changes in antihypertensive treatment in older adults; as hypertensive patients often require combination therapies for optimal blood pressure control, we focused on the number of antihypertensive drugs (active agents).

Methods

Data were taken from a seniors cohort, which was established in 2008–2010 with 2076 individuals selected through stratified random sampling from the non-institutionalized population aged ≥60 years in Spain.[15] In 2012–2013 (median follow-up period 3.5 years), updated data were collected. The study protocol was approved by a University Hospital Clinical Research Ethics Committee, and patients provided written informed consent.

Participants' sleep duration was obtained by asking: "How many minutes do you usually sleep per day (including both nighttime and daytime)?" Sleep quality was obtained by asking: "Do you have difficulty falling asleep?" and "Do you have difficulty staying asleep (night awakenings)?"; those who answered "sometimes" or "never or rarely" to the two questions were classified as having good sleep quality, and those who responded "usually" to any of the them as poor sleep quality. Participants were also asked: "Do you take medication to sleep?", with the following responses: "usually", "sometimes" and "never/rarely." The latter two responses were classified as "unusual."

Overall medication consumption was obtained by asking the participants: "How many medications do you currently use?", and by checking the number reported with the packages and medical prescriptions he/she had at home. Only antihypertensive drugs were selected for this analysis. The outcome variable was the change in the number of antihypertensive drugs (active agents),

which was calculated as the number of drugs in 2012–2013 minus the number in 2008–2010.

Baseline information on potential confounders of the associations was collected. Sociodemographic variables included age, sex and educational attainment (≤primary, secondary or university). Diet was assessed using a computerized dietary history validated in Spain. Total energy intake (kcal/day) was estimated, and the Mediterranean diet was approached by an adherence screener, which scores from 0 to 14 depending on the food consumed, quantity and frequency, with a higher score indicating better adherence. The Mediterranean diet adherence screener was classified into sex-specific tertiles. Total sodium and potassium intake was expressed in mmol/day. Alcohol consumption was obtained with the frequency–quantity scale used in the Spanish National Health Survey, and participants were classified as excessive drinkers (>24 g/day of alcohol intake in women, and >40 g/day in men) or non-excessive drinkers (never drinker, former drinker, moderate drinker). The following eight comorbidities were considered. Seven of them were self-reported chronic diseases diagnosed by the physician: asthma or chronic bronchitis, arthritis, osteoarthritis, hip fracture, depression (in need of treatment), cardiovascular disease (ischemic heart disease, stroke or heart failure) and cancer at any site; and diabetes mellitus was defined as fasting glucose ≥126 mg/dL or current treatment. Sleep apnea was self-reported based on physician diagnosis. Weight and height were measured using standardized procedures, and body mass index was calculated as weight (kg) divided by squared height (m^2). Blood pressure was measured three times using standardized conditions and validated devices. Hypertension control, both at baseline and at follow up, was considered if systolic blood pressure was <140 mmHg and diastolic blood pressure <90 mmHg.

Statistical analysis

The analyses were carried out with 752 participants who were treated with hypertensive drugs at baseline. The associations between each sleep characteristics (sleep duration in hours [continuous], sleep quality [poor/good], and sleeping pill consumption [usual/unusual]) in 2008–10 and the change in the number of antihypertensive drugs (increase or decrease/maintenance) from 2008–2010 to 2012–2013 were summarized with odds ratios (OR) and 95% confidence interval (CI) obtained from multiple logistic regression. Models were adjusted consecutively for baseline covariates (see Table 3 footnote).

Analyses were carried out using Stata/SE, version 13 (Stata Corp, College Station, TX, USA).

Results

At baseline, the participants' mean age was 69.9 ± 6.6 years), 49.2% were men, the mean sleep duration was 6.9 ± 1.4 h/day, 37.0% had poor sleep quality, 16.5% usually consumed sleeping pills and the mean number of antihypertensive drugs was 1.8 ± 0.9. During the follow-up period, 156 (20.7%) participants increased the number of antihypertensive drugs that they were taking.

Table 1 shows the baseline characteristics of participants according to their status of sleeping pills consumption in 2008–2010. Compared with patients who were not usual sleeping pills consumers, those who usually consumed sleeping pills were more frequently women, had significantly higher frequency of low educational level, lower energy consumption, higher frequency of comorbidities (≥2) and uncontrolled hypertension, they slept fewer hours a day, and had a higher frequency of poor sleep quality.

Table 2 shows the baseline characteristics of participants who increased and those who decreased/maintained the number of antihypertensive medications between 2008–2010 and 2012–2013. Compared with patients who decreased or maintained the number of antihypertensive drugs, those who increased this number had a higher mean number of comorbidities, slept fewer hours a day, more frequently took sleeping pills, and took a lower mean number of blood pressure medication and had higher frequency of uncontrolled hypertension.

No statistically significant association was found between the sleep duration or quality and the change in the number of antihypertensive drugs (Table 3). However, patients who usually took sleeping pills had an 85% higher risk of increasing the number of antihypertensive drugs than those who were not usual consumers (fully adjusted OR 1.85, 95% CI 1.12–3.07, $P = 0.017$).

Of the 124 participants who usually took sleeping pills in 2008–2010, 92 (74%) keep on the same "usually consuming" status in 2012–2013, and most (571% or 91%) of the 628 patients who were not usual consumers at baseline did not change their consumption status after follow up. As a sensitivity analysis, after additionally adjusting the association between sleeping pills consumption and increased antihypertensive drug consumption for the change in hypnotic consumption between 2008–2010 and 2012–2013, the association remained similar in magnitude and statistically significant (OR 1.77, 95% CI 1.06–2.95, *P*-value

Table 1 Baseline characteristics of treated hypertensive participants, according to the sleeping pills consumption in 2008–2010

Baseline characteristics	Sleeping pills consumption		
	Usual	Sometimes/never	*P*
n (%)	124 (16.5)	628 (83.5)	
Age, years (SD)	71.2 (6.9)	69.7 (6.5)	0.406
Men, *n* (%)	31 (25.0)	339 (53.9)	<0.001
Educational level (primary or less), *n* (%)	90 (72.6)	355 (56.5)	0.001
Non-excessive drinkers, *n* (%)	119 (95.9)	570 (90.7)	0.056
Energy intake kcal/day, mean (SD)	1832.6 (570.8)	2005.3 (557.8)	0.002
Mediterranean diet, mean score (SD)	7.0 (1.8)	7.3 (1.8)	0.417
Potassium intake (mmol/day), mean (SD)	0.06 (0.2)	0.08 (0.3)	0.404
Sodium intake (mmol/day), mean (SD)	109.4 (46.9)	118.2 (49.4)	0.070
Body mass index (kg/m^2), mean (SD)	29.8 (5.0)	29.6 (4.2)	0.588
Comorbidities, *n* (%)	53 (42.7)	140 (22.3)	<0.001
Sleep apnea syndrome, *n* (%)	4 (3.3)	29 (4.6)	0.505
Controlled hypertension, *n* (%)	41 (33.1)	270 (43.0)	0.040
No. antihypertensive drugs, mean (SD)	1.8 (0.9)	1.8 (0.9)	0.569
Sleep duration (h/day), mean (SD)	6.6 (1.6)	6.9 (1.4)	0.008
Poor sleep quality, *n* (%)	85 (68.6)	193 (30.7)	<0.001

SD, standard deviation.

Table 2 Baseline characteristics of treated hypertensive participants, according to the change in antihypertensive drugs between 2008–2010 and 2012–2013

Baseline characteristics	Change in the no. antihypertensive drugs		
	Increase	Decrease/maintenance	*P*
n (%)	156 (20.7)	596 (79.3)	
Age, years (SD)	70.8 (6.6)	69.8 (6.6)	0.434
Men, *n* (%)	80 (51.3)	290 (48.7)	0.559
Educational level (primary or less), *n* (%)	103 (66.0)	342 (57.4)	0.134
Non-excessive drinkers, *n* (%)	143 (91.7)	546 (91.6)	0.982
Energy intake (kcal/day), mean (SD)	1957.2 (551.8)	1981.9 (566.5)	0.626
Mediterranean diet, mean score (SD)	7.14 (1.8)	7.25 (1.8)	0.984
Potassium intake (mmol/day), mean (SD)	0.051 (0.22)	0.081 (0.27)	0.216
Sodium intake (mmol/day), mean SD)	115.1 (48.4)	117.2 (49.3)	0.646
Body mass index (kg/m^2), mean (SD)	29.8 (4.7)	29.6 (4.3)	0.627
Comorbidities, mean (SD)	1.2 (1.0)	1.0 (0.9)	0.002
Sleep apnea syndrome, *n* (%)	5 (3.2)	28 (4.7)	0.419
Controlled hypertension, *n* (%)	52 (33.3)	259 (43.5)	0.022
No. antihypertensive drugs, mean (SD)	1.5 (0.8)	1.9 (0.9)	<0.001
Sleep duration (h/day), mean (SD)	6.7 (1.5)	6.9 (1.4)	0.032
Poor sleep quality, *n* (%)	66 (42.3)	212 (35.6)	0.121
Usual sleeping pills consumption, *n* (%)	38 (24.4)	86 (14.4)	0.003

SD, standard deviation.

Table 3 Association between baseline sleep characteristics and the increase in antihypertensive drugs in 2008–2013

Baseline sleep characteristics	Increase of antihypertensive drugs between 2008 and 2013					
	Model 1		Model 2		Model 3	
	Odds ratio (95% CI)	*P*	Odds ratio (95% CI)	*P*	Odds ratio (95% CI)	*P*
Sleep duration (h/day)	0.88 (0.77–1.01)	0.077	0.87 (0.77–1.02)	0.086	0.91 (0.78–1.05)	0.185
Sleep quality (poor *vs* good)	1.02 (0.68–1.53)	0.911	1.03 (0.68–1.56)	0.879	1.07 (0.69–1.65)	0.769
Sleeping pills (usual *vs* unusual)	1.86 (1.16–2.98)	0.010	1.88 (1.16–3.04)	0.010	1.85 (1.12–3.07)	0.017

Model 1: Logistic regression model adjusted for age, sex and level of education; plus mutually adjusted for the other sleep characteristics. CI, confidence interval. Model 2: Logistic regression model adjusted as model 1 plus additionally adjusted for non-excessive drinking, energy intake, Mediterranean diet, potassium intake, sodium intake, body mass index and time dedicated to activities (walking, cycling/doing sport, gardening/DIY, housework, watching TV, playing PC, traveling by bus, reading, listening to music, having breakfast, lunch, dinner and napping). Model 3: Logistic regression model adjusted as model 2 plus additionally adjusted for number of comorbidities, sleep apnea syndrome, number of baseline antihypertensive drugs and control of hypertension in 2008 and 2013. Covariates were modeled as continuous except education (≤primary, secondary or university), non-excessive drinking (yes/no), sleep apnea (yes/no) and control of hypertension (yes/no).

0.028). Likewise, the OR for the association between sleep duration or sleep quality and change in blood pressure medication remained similar and non-statistically significant after this additional adjustment (OR 0.90, 95% CI 0.78–1.05, $P = 0.178$; and OR 1.05, 95% CI 0.68–1.63, $P = 0.822$, respectively).

Discussion

In the present study, usual consumption of sleeping pills was prospectively associated with a higher risk of increasing the number of antihypertensive drug treatments in older adults. Importantly, this association was observed regardless of sleep duration and quality, body mass index, diet, physical activity, and hypertension control.

The present findings of no association between sleep duration and quality and change in antihypertensive drug treatment in older adults are consistent with some studies that found no association between sleep characteristics and hypertension or hypertensive treatment in older adults.[7–9,11,12]. For example, in the Sleep Heart Health Study, antihypertensive treatment among hypertensive patients did not vary according to sleep duration.[9]

Our finding that habitual use of sleeping pills was associated with an increase in antihypertensive treatment might be partly explained by some factors. A number of studies have reported that some sleeping pills (e.g. benzodiazepine hypnotics) might increase sleep-disordered breathing in some cases, and sleep disorders might be associated with hypertension and, in particular, with nocturnal hypertension in older patients.[14,16–18] Also, some sleep medications (e.g. trazodone) have been shown to inhibit the hypotensive effect of various antihypertensive agents (e.g. clonidine, methyldopa) in animals, and hypertension has also occurred in a few patients during long-term therapy, yet the clinical importance of this potential interaction has not been determined;[19] unfortunately, we did not have detailed data on hypnotic types for most of the present patients, but it seems that the consumption of these drugs was low. Other potential reasons of the association include underlying sleep disturbances not examined in this report (e.g. anxiety) and reduced physical activity (self-reported in this study) because of sedation, which is related to hypertension.[1]

Among study limitations, we lacked data on long-term patterns of sleep characteristics and covariates, and some changes over time are possible. Also, sleep data were self-reported; however, these variables have shown adequate validity.[20] Residual confounding might also still exist because data on some variables were not precise enough (e.g. sleep quality was dichotomized) or because of unmeasured or insufficiently adjusted confounders. Finally, although reverse causation cannot be entirely ruled out, the present study design and adjustment for baseline antihypertensive treatment limits this possibility.

In conclusion, the present prospective study of older hypertensive patients shows an independent association between usual sleeping pills consumption and an increasing number of blood pressure medications over time. The importance of this study

from a clinical viewpoint is not just the association between sleeping pill use and future need of antihypertensive drugs, but the importance of taking "sleeping pill use" as a "warning indicator" to investigate the underlying sleep disorders or unhealthy lifestyles. However, further studies are required to confirm this association and elucidate underlying mechanisms. These findings are important given that one in five older people in the present study increased their antihypertensive treatments during the follow-up period, and it is known that the greater the number of medications patients take, the higher the risk of inadequate medications, adverse reactions and lower treatment adherence.[21]

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Disclosure statement

The authors declare no conflict of interest.

References

1 Aronow WS, Fleg JL, Pepine CJ *et al*. ACCF/AHA 2011 expert consensus document on hypertension in the elderly: a report of the American College of Cardiology Foundation Task Force on Clinical Expert Consensus documents developed in collaboration with the American Academy of Neurology, American Geriatrics Society, American Society for Preventive Cardiology, American Society of Hypertension, American Society of Nephrology, Association of Black Cardiologists, and European Society of Hypertension. *J Am Coll Cardiol* 2011; **57**: 2037–2114.
2 Beckett N, Peters R, Tuomilehto J *et al*. Immediate and late benefits of treating very elderly people with hypertension: results from active treatment extension to hypertension in the very elderly randomised controlled trial. *BMJ* 2011; **344**: d7541.
3 Qaseem A, Wilt TJ, Rich R *et al*. Pharmacologic treatment of hypertension in adults aged 60 years or older to higher versus lower blood pressure targets: a clinical practice guideline from the American College of Physicians and the American Academy of family physicians. *Ann Intern Med* 2017; **166**: 430–437.
4 Crowley K. Sleep and sleep disorders in older adults. *Neuropsychol Rev* 2011; **21**: 41–53.
5 Knutson KL, Van Cauter E, Rathouz PJ *et al*. Association between sleep and blood pressure in midlife: the CARDIA sleep study. *Arch Intern Med* 2009; **169**: 1055–1061.
6 Gangwisch JE, Heymsfield SB, Boden-Albala B *et al*. Short sleep duration as a risk factor for hypertension: analyses of the first National Health and Nutrition Examination Survey. *Hypertension* 2006; **47**: 833–839.
7 St-Onge MP, Grandner MA, Brown D *et al*. Sleep duration and quality: impact on lifestyle behaviors and cardiometabolic health: a scientific statement from the American Heart Association. *Circulation* 2016; **134**: e367–e386.
8 Spiegelhalder K, Scholtes C, Riemann D. The association between insomnia and cardiovascular diseases. *Nat Sci Sleep* 2010; **2**: 71–78.
9 Gottlieb DJ, Redline S, Nieto FJ *et al*. Association of usual sleep duration with hypertension: the Sleep Heart Health Study. *Sleep* 2006; **29**: 1009–1014.
10 Vgontzas AN, Liao D, Bixler EO, Chrousos GP, Vela-Bueno A. Insomnia with objective short sleep duration is associated with a high risk for hypertension. *Sleep* 2009; **32**: 491–497.
11 van den Berg JF, Tulen JH, Neven AK *et al*. Sleep duration and hypertension are not associated in the elderly. *Hypertension* 2007; **50**: 585–589.
12 Lopez-Garcia E, Faubel R, Guallar-Castillon P, Leon-MuÃ±oz L, Banegas JR, Rodriguez-Artalejo F. Self-reported sleep duration and hypertension in older Spanish adults. *J Am Geriatr Soc* 2009; **57**: 663–668.
13 Banegas JR, Navarro-Vidal B, Ruilope LM *et al*. Trends in hypertension control among the older population of Spain from 2000 to 2001 to 2008 to 2010: role of frequency and intensity of drug treatment. *Circ Cardiovasc Qual Outcomes* 2015; **8**: 67–76.
14 Petrov ME, Howard VJ, Kleindorfer D, Grandner MA, Molano JR, Howard G. Over-the-counter and prescription sleep medication and incident stroke: the REasons for Geographic and Racial Differences in Stroke study. *J Stroke Cerebrovasc Dis* 2014; **23**: 2110–2116.
15 Rodríguez-Artalejo F, Graciani A, Guallar-Castillon P *et al*. Rationale and methods of the study on nutrition and cardiovascular risk in Spain (ENRICA). *Rev Esp Cardiol* 2011; **64**: 876–882.
16 Chung S, Youn S. The optimizing strategies for prescription of sleeping pills for insomnia patients. *Sleep Med Res* 2017; **8**: 8–16.
17 Yaggi HK, Concato J, Kernan WN, Lichtman JH, Brass LM, Mohsenin V. Obstructive sleep apnea as a risk factor for stroke and death. *N Engl J Med* 2005; **353**: 2034–2041.
18 Morley JE, Sanford A, Bourey R. Sleep apnea: a geriatric syndrome. *J Am Med Dir Assoc* 2017; **18**: 899–904.
19 American Society of Health-System Pharmacists 2015. *Drug Information 2015*. Bethesda, MD: ASHP (American Society of Health-System Pharmacists), 2015; 2379–2380.
20 Lauderdale DS, Knutson KL, Yan LL, Liu K, Rathouz PJ. Self-reported and measured sleep duration: how similar are they? The CARDIA Sleep Study. *Epidemiology* 2008; **19**: 838–845.
21 Salazar JA, Poon I, Nair M. Clinical consequences of polypharmacy in elderly: expect the unexpected, think the unthinkable. *Expert Opin Drug Saf* 2007; **6**: 695–704.

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