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ORIGINAL STUDY

Association between weekend catch-up sleep and hyperuricemia with insufficient sleep in postmenopausal Korean women: a nationwide cross-sectional study

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Abstract

Objective: Hyperuricemia is associated with metabolic and cardiovascular diseases and mortality. Efforts to lower the risk of hyperuricemia in various ways are needed as the prevalence of these diseases increases in postmenopausal women. Studies have shown that one of these methods is associated with adequate sleep duration, which is related to a low risk of hyperuricemia. Considering that it is difficult for people to get enough sleep in modern society, this study hypothesized that weekend catch-up sleep could be an alternative. To our knowledge, no past study has investigated the relation between weekend catch-up sleep and hyperuricemia in postmenopausal women. Hence, the aim of this research was to estimate the relation between weekend catch-up sleep and hyperuricemia with insufficient sleep in postmenopausal women during weekday or workday.

Methods: This study included 1,877 participants extracted from the Korea National Health and Nutrition Examination Survey VII. The study population was divided into weekend catch-up sleep and non–weekend catch-up sleep groups. Odds ratios with 95% confidence intervals were derived using multiple logistic regression analysis.

Results: Weekend catch-up sleep had a significantly lower prevalence of hyperuricemia after adjusting for confounders (odds ratio, 0.758 [95% confidence interval, 0.576-0.997]). In a subgroup analysis, weekend catch-up sleep of 1 to 2 hours was significantly correlated with a lower prevalence of hyperuricemia after adjusting for confounders (odds ratio: 0.522 [95% confidence interval, 0.323-0.845]).

Conclusions: Weekend catch-up sleep had a decreased prevalence of hyperuricemia in postmenopausal women with sleep deprivation.

Key Words: Cardiovascular disease – Menopause – Sleep recovery – Sleep restriction – Uricemia.

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Uric acid is the product of purine metabolism, which causes hyperuricemia when the balance between its synthesis and excretion is broken.[1] Along with inflammatory conditions caused by urate crystal deposits,[2] hyperuricemia has harmful effects as a pro-oxidant that increases oxidative stress or as a risk-related molecular pattern that causes systemic inflammation, mainly in the vascular wall.[3] Consequently, hyperuricemia is not limited to gout but is known to be associated with obesity, diabetes mellitus, hypertension, metabolic syndrome, cardiovascular disease (CVD), and mortality.[3–5] Hyperuricemia gradually increases with increasing age in all populations, and its prevalence increases especially after menopause.[6,7] According to previous studies, hyperuricemia, which can be recognized as a risk factor for CVD,[8] is inversely related to estrogen levels.[9]

In fact, hormone therapy lowered the CVD risk in postmenopause; therefore, it is a recommended treatment in some cases, but it cannot be targeted to all postmenopausal women because of various adverse effects.[10,11] Hence, a multidimensional approach is required in addition to hormone therapy.

It is quite clear that sleep is essential for many people's development, immune response, cognition, performance, psychological state, and disease.[12] According to several studies, too little or too much sleep is related to poor health problems, including hyperlipidemia, hypertension, type 2 diabetes, hyperuricemia, obesity, CVD, and even total mortality.[13–15] In this context, Chaput et al[16] showed that the best-associated sleep time for health in adults was 7 to 8 hours per day. Sleep deprivation, however, is common in modern society.[14,17] Weekend catch-up sleep (WCUS), which replenishes sleep debt during weeks or workdays, may be useful to compensate for sleep restriction during the week. Although a study reported that there were no metabolic advantages in catch-up sleep,[18] many researchers have reported that WCUS is associated with a lower risk of hypertension,[19,20] obesity,[21] and type 2 diabetes.[22]

The objectives of this research were to identify the association between WCUS and hyperuricemia in postmenopausal women with insufficient sleep duration and to determine whether WCUS can be another way to reduce hyperuricemia in Korean postmenopausal women.

METHODS

Participants

This study extracted data from participants of the seventh Korea National Health and Nutrition Examination Survey (KNHANES) from 2016 to 2018. This is a national, cross-sectional, population-based survey and has been operated by the Korea Disease Control and Prevention Agency annually. The survey included a random sample of 23 households in 192 regions and examined household members older than 1 year. These examinations included health interviews, nutrition surveys, data collected via questionnaires, standardized physical examinations, and blood/urine tests.

The participants were postmenopausal women who slept for an average of less than 7 hours per day. For optimal health in adults, more than 7 hours of average sleep per day is recommended according to the American Academy of Sleep Medicine and Sleep Research Society.[23] Therefore, participants with less than 7 hours of sleep per day were considered a sleep restriction group. Of the 24,269 participants from the seventh KNHANES, those diagnosed with any types of carcinoma, such as thyroid, liver, stomach, colon, breast, cervix, and other cancers, were excluded. In addition, workers who worked during different shifts and those with no relevant data were excluded (Fig. 1). The present study was approved by the Institutional Review Board of Pusan National University Yangsan Hospital (IRB No. 05-2022-186).

Measures

Study variables

A survey was conducted on all participants to obtain information about their age, income, marital status, smoking and alcohol intake, and physical activity. Personal income was classified into quartiles according to the KNHANES, and among them, high-middle and high quartiles were regarded as high income, and low-middle and low quartiles were considered as low income. Participants were categorized as married or single and as current smokers or nonsmokers. In addition, participants were considered as a drinker if the frequency of drinking was more than once a month in the previous year. Regular aerobic physical activity was indicated as moderate-intensity physical activity for at least 2.5 hours weekly, high-intensity physical activity for at least 1.5 hours, or mixed moderate-intensity and high-intensity physical activity (1 min of high-intensity is considered to be 2 min of moderate-intensity).

Participants were deemed to have hypertension if their blood pressure was increased (systolic ≥140 mm Hg or diastolic ≥90 mm Hg), or if they were treated for hypertension. Participants were found to have diabetes if their glucose level was elevated after more than 8 hours of fasting (fasting blood glucose ≥126 mg/dL) or if they were taking diabetes medication. Participants were considered to have hyperlipidemia if their total cholesterol was increased (≥240 mg/dL) or if they were treated for hyperlipidemia according to the KNHANES definition. Obesity was defined, based on the World Health Organization guidelines for Asians,[24] as a body mass index of at least 25 kg/m^2. Based on the modified National Cholesterol Education Panel Adult Treatment Panel III, metabolic syndrome defined as more than three of the following traits[25]: (1) increased waist circumference (≥90 cm for men, ≥85 cm for women) and/or (2) high blood pressure (systolic ≥135 mm Hg or diastolic ≥85 mm Hg) or taking antihypertensive drugs and/or (3) elevated triglyceride (≥150 mg/dL) or medication for hyperlipidemia and/or (4) reduced high-density lipoprotein cholesterol (<50 mg/dL for women, <40 mg/dL for men) and/or (5) high fasting blood glucose (≥100 mg/dL) or antidiabetic treatment. Finally, this study defined CVD as a history of angina, myocardial infarction, or stroke.

Weekend catch-up sleep

Based on responses from the questionnaires, WCUS was obtained using the average sleep duration of weekdays (or workdays) and weekends (or free days). The WCUS value was calculated by subtracting the average weekday sleep duration per day from the average weekend sleep duration per day.[26] Then, the participants were divided into the WCUS and non-WCUS (meaning WCUS ≤0 h) groups.

Hyperuricemia

The blood samples of the participants who visited the designated regional institution were collected and put into serum separating tube bottles with the participant's unique number. The samples were refrigerated (2°C-8°C) equipped with a digital thermometer and GPS. A transportation officer visited to collect samples in time for the examination date, and the collected samples were transported to the central examination center on the same day (Seoul, Republic of Korea). Samples are regularly checked for contamination or completeness of collection for quality control (Korea Ministry of Health and Welfare).

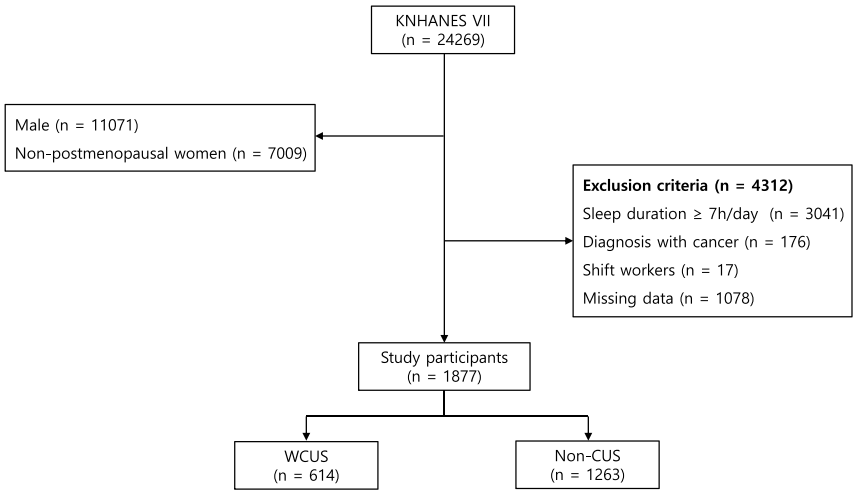

FIG. 1. Flow diagram of study participants in KNHANES VII. KNHANES, Korean National Health and Nutrition Examination Survey; *n*, number; non-WCUS, non–weekend catch-up sleep; WCUS, weekend catch-up sleep.

Serum uric acid was measured using an automatic analyzer 7600-210 (Hitachi, Tokyo, Japan). In women, hyperuricemia refers to a serum uric acid level of at least 6 mg/dL.[3]

Statistical analyses

A complex sampling design, including integrated weights, stratification, and clusters suggested in the guidelines for analyzing data from the seventh KNHANES, was used to identify nationwide representative samples.

The baseline characteristics of the participants were estimated using the *t* test and χ^2 test. Data are shown as mean ± SD for continuous variables or as number and percentages for categorical variables. To identify the relationship between WCUS and hyperuricemia, multiple logistic regression was carried out after adjusting for the following potential confounders: (i) age, (ii) current smoking status, (iii) alcohol intake, (iv) physical activity, (v) hypertension, (vi) diabetes, (vii) hyperlipidemia, (viii) obesity, (ix) metabolic syndrome, and (x) CVDs. Multiple logistic regression was performed after adjusting for the same confounding factors mentioned previously to investigate the prevalence of hyperuricemia according to WCUS duration. All statistical analyses were performed using the IBM SPSS version 21 (Armonk, NY). A $P < 0.05$ considered statistically significant.

RESULTS

Baseline characteristics of the participants

Of the 24,269 people, after men (11,071) and nonmenopausal women (7,009) were excluded, 6,189 participants remained. Then, excluding 4,312 who met the exclusion criteria, 1,877 were selected as participants (Fig. 1). The WCUS and non-WCUS groups comprised 614 and 1,263 participants, respectively.

The characteristics of the study population are presented in Table 1. The overall mean age of WCUS group was lower than that of the non-WCUS group (non-WCUS, 65.21 ± 0.173 y; WCUS, 59.39 ± 0.234 y; $P < 0.001$). The number of participants with hyperuricemia was significantly higher in the non-WCUS than in the WCUS. The rates of physical activity in the WCUS were significantly higher than in the non-WCUS. The WCUS group periodically drank at a significantly higher rate than the non-WCUS group did. Socioeconomic indicators, income status, and marital status were significantly higher in the WCUS group. The morbidity of hypertension, diabetes, metabolic syndrome, and CVD was significantly lower in the WCUS. The WCUS group, however, showed no significant difference in the prevalence of hyperlipidemia and obesity compared with non-WCUS.

Association between WCUS and hyperuricemia

A multiple logistic regression analysis was performed to evaluate if there was a significant association between WCUS and hyperuricemia (Table 2). Participants with WCUS had a significantly decreased prevalence of hyperuricemia (odds ratio [OR], 0.592 [95% confidence interval {CI}, 0.459-0.764]). After adjusting for potential confounders, including age, smoking status, alcohol consumption, physical activity, hypertension, diabetes, hyperlipidemia, obesity, metabolic syndrome, and CVD, WCUS was found to be associated significantly with decreased prevalence of hyperuricemia (OR, 0.758 [95% CI, 0.576-0.997]).

Association between WCUS and hyperuricemia by WCUS duration

In addition, multiple logistic regression analysis was carried out to investigate the extent to which WCUS should be performed to reduce the prevalence of hyperuricemia by dividing the WCUS group as follows: WCUS ≤0 hours (non-WCUS, reference), 0 < WCUS ≤ 1 hour, 1 < WCUS < 2 hours, and WCUS ≥2 hours (Table 3). Participants with WCUS showed a significantly lower prevalence of hyperuricemia in WCUS of 0 to 2 hours (0 < WCUS ≤ 1: OR, 0.633 [95% CI, 0.452-0.886]; 1 < WCUS < 2: OR, 0.392 [95% CI, 0.248-0.620]). After adjusting for confounders, including age, current smoking status, alcohol intake, physical activity, hypertension, diabetes, hyperlipidemia, obesity, metabolic syndrome, and CVD, WCUS of 1 to 2 hours was significantly related to a lower prevalence of hyperuricemia (1 < WCUS < 2: OR, 0.522 [95% CI, 0.323-0.845]).

TABLE 1. *Baseline characteristics of study participants*

Characteristic	*N*	Non-WCUS (*n* = 1,263)	WCUS (*n* = 614)	*P*[a]
Age, y		65.21 ± 0.173	59.39 ± 0.234	<0.001[b]
Current smoker, *n* (%)	1,874			<0.001
Smoker		68 (5.4)	23 (3.8)	
Nonsmoker		1,194 (94.6)	589 (96.2)	
Drinking[c], *n* (%)	1,873			<0.001
Yes		612 (48.5)	353 (57.7)	
No		649 (51.5)	259 (42.3)	
Physical activity[d], *n* (%)	1,868			0.009
Yes		426 (33.9)	248 (40.5)	
No		829 (66.1)	365 (59.5)	
Income[e], *n* (%)	1,869			<0.001
High		611 (48.6)	348 (56.8)	
Low		645 (51.4)	265 (43.2)	
Marital status, *n* (%)	1,877			0.003
Married		1,241 (98.3)	606 (98.7)	
Unmarried		22 (1.7)	8 (1.3)	
Hypertension, *n* (%)	1,874			<0.001
Yes		657 (52.1)	245 (40.0)	
No		604 (47.9)	368 (60.0)	
Diabetes, *n* (%)	1,810			<0.001
Yes		252 (20.8)	78 (13.1)	
No		962 (79.2)	518 (86.9)	
Hyperlipidemia, *n* (%)	1,817			0.085
Yes		513 (42.1)	239 (39.9)	
No		705 (57.9)	360 (60.1)	
Obesity[f], *n* (%)	1,870			0.091
Yes		505 (40.1)	229 (37.5)	
No		754 (59.9)	382 (62.5)	
Metabolic syndrome, *n* (%)	1,877			<0.001
Yes		621 (49.2)	242 (39.4)	
No		642 (50.8)	372 (60.6)	
CVD[g], *n* (%)	1,877			0.012
Yes		96 (7.6)	29 (4.7)	
No		1,167 (92.4)	585 (95.3)	
Hyperuricemia[h], *n* (%)	1,796			<0.001
Yes		126 (10.5)	34 (5.7)	
No		1,077 (89.5)	559 (94.3)	

Values are presented as number (percentage) or mean ± standard deviation. Non-WCUS means WCUS ≤0 hour.
CVD, cardiovascular disease; *n*, number; non-WCUS, non–weekend catch-up sleep; WCUS, weekend catch-up sleep.
[a]Based on χ^2 test ($P < 0.05$).
[b]Based on *t* test ($P < 0.05$).
[c]Average drinking frequency is more than once a month in the past year.
[d]Moderate-intensity physical activities for more than 2.5 hours a week, high-intensity physical activities for more than 1.5 hours, or mix medium-intensity and high-intensity physical activities (1 min of high-intensity is considered to be 2 min of moderate-intensity).
[e]Consider high and high-middle as high, and low and low-middle as low classified according to the quartile of KNHANES.
[f]Body mass index is more than 25 kg/m^2.
[g]Cardiovascular disease refers to the current prevalence of angina or myocardial infarction or stroke.
[h]Hyperuricemia: serum uric acid ≥6 mg/dL (in women).

TABLE 2. *Association between WCUS and hyperuricemia (serum uric acid ≥6 mg/dL)*

	Model 1	Model 2
WCUS		
Non-WCUS	Reference	Reference
CUS	0.592 (0.459-0.764)[a]	0.758 (0.576-0.997)[a]

Values are presented as odds ratio (95% confidence interval). Model 1 was unadjusted; model 2 was adjusted for age, current smoking status, alcohol intake, physical activity, hypertension, diabetes, hyperlipidemia, obesity, metabolic syndrome, and cardiovascular disease (angina pectoris, myocardial infarction, stroke).
CUS, catch-up sleep; non-WCUS, non–weekend catch-up sleep; WCUS, weekend catch-up sleep.
[a]$P < 0.05$.

TABLE 3. *Association between WCUS and hyperuricemia (serum uric acid ≥6 mg/dL) by CUS duration*

	Model 1	Model 2
WCUS		
≤0 h (non-WCUS)	Reference	Reference
0 < CUS ≤ 1 h	0.633 (0.452-0.886)[a]	0.754 (0.526-1.082)
1 < CUS < 2 h	0.392 (0.248-0.620)[a]	0.522 (0.323-0.845)[a]
≥2 h	0.653 (0.426-1.001)	0.909 (0.580-1.423)

Values are presented as odds ratio (95% confidence interval). Model 1 was unadjusted; model 2 was adjusted for age, current smoking status, alcohol intake, physical activity, hypertension, diabetes, hyperlipidemia, obesity, metabolic syndrome, and cardiovascular disease (angina pectoris, myocardial infarction, stroke).
CUS, catch-up sleep; non-WCUS, non–weekend catch-up sleep; WCUS, weekend catch-up sleep.
[a]$P < 0.05$.

WCUS of 0 to 1 hour and greater than 2 hours were not statistically significant (0 < WCUS ≤ 1: OR, 0.754 [95% CI, 0.526-1.082]; WCUS ≥2: OR, 0.909 [95% CI, 0.580-1.423]).

DISCUSSION

This study examined the association between WCUS and hyperuricemia with sleep deprivation in postmenopausal women. Participants with WCUS showed a significantly lower prevalence of hyperuricemia even after adjusting for potential confounding factors. In particular, the prevalence of hyperuricemia was significantly lowered at WCUS 1 to 2 hours.

Contrary to the effects of sleep deprivation, sleep supplementation may be related to several mechanisms that lower hyperuricemia. First, WCUS may restore inflammatory reactions and normal endothelial function. Although the mechanisms are not fully understood, sleep loss and high uric acid levels are associated with inflammatory response and endothelial dysfunction, respectively. A systemic review showed that sleep restriction increases reactive oxygen species production and the vascular inflammatory response, damaging the microvascular and macrovascular endothelium and causing the progression of hypertension, atherosclerosis, and renal diseases.[27] In addition, experimental studies have shown that high uric acid levels increase inflammatory responses.[1] Furthermore, several clinical studies have reported that hyperuricemia induces endothelial dysfunction and is a causal risk factor.[1,28] Sleep restriction and hyperuricemia are related because several studies have shown that short sleep duration increases the risk of obesity, metabolic syndrome, and hypertension, which are risk factors for hyperuricemia.[29] Although the molecular mechanism by which sleep extension lowers uric acid levels has not yet been fully identified, Jung et al[30] suggested that WCUS lowers serum high-sensitivity C-reactive protein levels, which is known as a marker of inflammation, and the risk of CVD. They reported that participants who had 1 to 2 hours of WCUS had a significantly decreased risk of high-sensitivity C-reactive protein than those with no WCUS. Similarly, the present study showed that participants who WCUS 1 to 2 hours had a significantly lower prevalence of hyperuricemia.

Similar to the first hypothesis, it can also be explained by insulin resistance in terms of metabolism. Several studies have shown that sleep deprivation reduces insulin sensitivity.[31,32] Although it is controversial whether hyperuricemia is the cause of diabetes, high uric acid levels damage glucose tolerance and increase insulin resistance. As mentioned earlier, sleep deprivation and hyperuricemia are related; therefore, WCUS, which compensates for sleep deprivation, can also reduce serum uric acid levels regarding insulin sensitivity. Leproult et al[33] reported that when participants who were nonobese healthy adults extended their sleep for 6 weeks after 2 weeks following their habitual bedtime (≤7 h of sleep), sleep extension affected improvement in insulin sensitivity at the serum level. The study by Killick et al[34] also showed improvement in insulin sensitivity during 3 weeks of sleep extension with sustained sleep restriction during the working week for at least 6 months.

Hyperuricemia may be improved by WCUS in postmenopausal women with reduced ovarian hormones, especially estradiol. Postmenopause is a risk factor for CVD. This is due to hormonal changes in the prevalence of vascular and metabolic diseases after menopause.[35] Studies have shown that the morbidity of CVDs is lower in premenopausal women than in men but increases in postmenopausal women, as much as in men, because of the loss of the hormonal protective effects of endothelial dysfunction, which hinders atherosclerosis and CVD.[36] In addition, because estradiol lowers serum uric acid levels by renal clearance, secretion, and reabsorption, postmenopausal women with low ovarian hormone levels have high uric acid levels.[37] A study reported that estradiol changes according to sleep patterns. Michels et al[38] found a decrease in average estradiol in women with sleep less than 7 hours per day. On the other hand, estradiol increased by 3.9% as sleep increased by an hour on average. Therefore, sleep recovery may lower serum uric acid levels because of increased estradiol levels in postmenopausal women.

This study had several limitations. First, the causal relationship between WCUS and hyperuricemia could not be clarified. Second, self-reported data on sleep duration may be less accurate than the measurements. Third, it was difficult to check information such as the prevalence of and use of urate-lowering treatment, sleep quality, and sleep disorders, such as sleep apnea and insomnia. Fourth, no experimental evidence exists that WCUS affects serum uric acid levels in postmenopausal women. Further experimental and clinical studies are required to elucidate this mechanism. This study, however, represents the general population of South Korea. As far as we know, this is the first study to investigate an association between WCUS and hyperuricemia in postmenopausal women.

CONCLUSIONS

The present study identified that WCUS is associated with a lower prevalence of hyperuricemia in Korean postmenopausal women with insufficient sleep. In addition, maintaining good sleep duration benefits hyperuricemia, a risk factor for metabolic and CVDs. If this is not possible, WCUS could be an alternative. Further studies, however, are required to identify the causal relationship between sleep recovery and hyperuricemia in postmenopausal women.

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