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Original Article

Quantitative association between nocturnal voiding frequency and objective sleep quality in the general elderly population: the HEIJO-KYO cohort

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ABSTRACT

Objective: A significant association between nocturia and subjective sleep quality has previously been reported; however, the association between nocturia and objective sleep quality remains unclear. The purpose of this study was to evaluate the quantitative association between nocturnal voiding (NV) frequency and objective sleep quality in a large, general, elderly population.
Methods: Nocturnal voiding frequency, objective sleep quality, and subjective sleep quality were measured among 1086 community-based elderly individuals using actigraphy and the Pittsburgh Sleep Quality Index (PSQI) questionnaire.
Results: In multivariate analyses adjusted for potential confounding factors (such as age, gender, body mass index, medication use, renal function, bedtime, rising time, daytime physical activity, endogenous melatonin levels, and bedroom light levels), increased NV frequency, ranging from zero, one, two, three or more voids, was significantly associated with poorer objective sleep quality, including lower sleep efficiency (SE) and longer wake after sleep onset (WASO) (mean SE, 86.3, 84.8, 83.6, and 81.2%, respectively; p for trend <0.001; mean WASO: 42.6, 49.0, 53.6, and 66.1 min, respectively; p for trend <0.001), but shorter sleep onset latency (SOL) (mean SOL, 3.0, 3.0, 2.8, and 2.8 log min, respectively; p for trend = 0.018). In addition, an increased NV frequency was significantly associated with poorer subjective sleep quality in a multivariate model (mean PSQI global score, 4.60, 4.86, 5.22, and 5.48, respectively; p for trend 0.012).
Conclusion: The present study revealed a quantitative association between NV frequency and objective sleep quality in the general elderly population.

1. Introduction

Previous epidemiological studies have revealed that the prevalence of self-reported sleep problems increases with age, and that up to 40% of elderly individuals suffer from problems related to the initiation and maintenance of sleep [1–4]. Sleep problems have commonly been associated with an increased risk of depression, dementia, cardiovascular diseases, and mortality [5–8]. Therefore, sleep problems in elderly individuals are important public health issues.

Nocturnal voiding (NV) frequency increases with age, and >20% of elderly individuals have two or more nocturnal voids [9,10]. An increased frequency of nocturnal voiding is a risk factor for both bone fractures and cardiovascular disease [11,12]. Although the International Continence Society defines nocturia as a condition in which the affected individual wakes one or more times at night to void, it remains unclear as to whether there is a quantitative association between NV frequency and pathophysiological significance [13].

Several previous studies have reported a significant association between nocturia and sleep quality; however, most of these studies characterized nocturia using a cutoff point of NV frequency, and sleep quality was assessed using self-reported questionnaires [10,14–17]. Although some inconsistency between subjective and objective sleep measures has been reported, the association between nocturia and objective sleep quality remains unclear [18]. A recent study suggested that there is a quantitative association between NV frequency, ranging from zero to four or more, and sleep quality measured actigraphically; however, the study was limited to generalizability of the findings because it included a small sample size ($n = 60$) and targeted a population with insomnia [19]. Therefore, the quantitative association between NV frequency and objective sleep quality should be evaluated in a large, general, elderly population.

In this cross-sectional study of 1086 community-dwelling elderly individuals, the association of continuous and categorical data on

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NV frequency with objective and subjective sleep quality using actigraphy and Pittsburgh Sleep Quality Index (PSQI) questionnaires was investigated.

2. Participants and methods

2.1. Participants and study protocol

A total of 1127 community-based elderly individuals aged ≥60 years were voluntarily enrolled into the study Housing environments and health investigation among Japanese older people in Nara, Kansai Region: a prospective community-based cohort (HEIJO-KYO) study between September 2010 and March 2014. Among these, 1086 participants met the inclusion criterion of having completed sleep quality and NV frequency measurements. All participants provided written, informed consent to participate in the study. The Nara Medical University Ethics Committee approved the study protocol.

The study protocols were previously described [20]. Briefly: demographic and medical information was collected using a standardized questionnaire, and measurements (including actigraphic parameters) were taken on two consecutive days. The participants were then instructed to collect urine samples the following night, maintain standardized sleep and urination diaries, and not to consume any alcohol during the monitoring period.

2.2. Measuring objective sleep quality

An actigraph (Actiwatch 2; Respironics Inc., PA, USA), worn on the non-dominant wrist, was used to measure objective sleep quality at 1-min intervals on two consecutive nights. The asleep/awake status at each epoch, sleep onset, and sleep offset were detected automatically using Actiware version 5.5 (Respironics) using the default algorithm [21]. Epochs with activity counts higher than a moderate threshold (40 counts/min) were treated as being awake. Sleep onset was defined as the first minute that was followed by a 10-min immobility period that contained not more than one epoch with any motion count. Sleep offset was defined as the last minute following a 10-min immobility period.

Objective data (awake/asleep status and sleep onset/offset) and self-reported data (bedtime and rising time) were used to calculate four actigraphic sleep parameters each night: (1) total sleep time (TST), the total time spent asleep (below the activity threshold of 40 counts/min) between sleep onset and offset; (2) sleep efficiency (SE), the %TST divided by the time between bedtime and rising time, as derived from the self-reported sleep diary; (3) wake after sleep onset (WASO), the time spent awake (above the activity threshold of 40 counts/min) between the sleep onset and rising times; and (4) sleep onset latency (SOL), the time between bedtime and sleep onset. Probable sleep-disordered breathing (SDB) was defined as an SE <70% and/or a TST <5 h because the odds ratio for SDB was significantly higher in the elderly population with these criteria [22].

2.3. Measuring subjective sleep quality

Subjective sleep quality was measured using PSQI questionnaires. Specifically, sleep quality over the previous month was determined using seven subscales that measure different components of sleep: sleep quality, latency, duration, efficiency, disturbance, sleep medication use, and daytime dysfunction. Each component was scored from 0 to 3, with 3 indicating the worst quality of sleep [23].

2.4. Measuring nocturnal voiding frequency

Nocturnal voiding frequency, except for the last void at bedtime and the first void in the morning, was logged using a standardized urination diary. In the first 189 participants, the correlation of NV frequency over four months was assessed. The agreement for two or more NVs between the two data sets was moderate (Kappa coefficient = 0.55).

2.5. Other measurements

Body mass index (BMI) was calculated as weight divided by the square of height in meters (kg/m^2). The use of antihypertensive drugs and sleep medications, and benign prostatic hyperplasia (BPH) were evaluated using a questionnaire. Diabetes mellitus was defined according to: medical history, the current use of antidiabetic agents, fasting plasma glucose levels, and plasma glycated hemoglobin levels. The estimated glomerular filtration rate (eGFR) was calculated using the formula described by the Japanese Society of Nephrology, Chronic Kidney Disease Practice Guide. Daytime physical activity was calculated as the mean physical activity over the two days, which was evaluated using an actigraph (Actiwatch 2; Respironics Inc., PA, USA) from rising time to bedtime. Endogenous melatonin levels were estimated according to nocturnal urinary 6-sulfatoxymelatonin excretion (UME) using a highly sensitive enzyme-linked immunosorbent assay (ELISA) kit (RE54031; IBL International, Hamburg, Germany) as previously described [20]. Bedroom light intensity was measured at 1-min intervals over two consecutive nights using a portable light meter (LX-28SD; Sato Shouji Inc., Kanagawa, Japan); the mean light intensity from bedtime to rising time was used to define the bedroom light intensity.

2.6. Statistical analyses

Age, gender, BMI, antihypertensive drugs and sleep medication use, diabetes, eGFR, bedtime, rising time, daytime physical activity, UME, and bedroom light intensity were included as independent variables. The mean values for daytime physical activity, bedtime, rising time, bedroom light intensity, and actigraphic sleep parameters on two consecutive days were used for analyses. The UME and SOL had a skewed distribution, and therefore, they were naturally log-transformed for analyses. Trends in the association between NV frequency and the independent variables and sleep parameters were evaluated using linear or logistic regression models when variables were normally distributed or categorical data, respectively. Jonckheere–Terpstra tests for trends were used when variables were distributed asymmetrically. Independent variables were adjusted in multivariate models to assess the association between NV frequency and sleep quality using analysis of covariance (ANCOVA) where there was no serious multicollinearity (all variance inflation factors <10). Antihypertensive drug use, which was significantly associated with NV frequency, was analyzed as a covariate in multivariate analyses. Sleep medication use was excluded from covariates in the multivariate analysis of subjective sleep measures because information regarding the use of sleep medication was included in the PSQI. Statistical analyses were performed using SPSS version 19.0 for Windows (IBM SPSS Inc., IL, USA). A two-tailed p-value of <0.05 was considered to be statistically significant.

3. Results

The mean age of the study participants was 71.8 ± 7.1 (standard deviation, SD) years, and 511 (47.1%) were male. Of the 1086 participants, 302 had zero NV, 462 had one NV, 232 had two NVs, and 90 had three or more NVs. Older age, male gender, calcium channel blocker (CCB) and sleep medication use, lower eGFR, earlier bedtime, later rising time, and lower daytime physical activity were significantly associated with increased NV frequency (Table 1). Probable SDB ($n = 66$) did not differ significantly according to NV frequency ($p_{trend} = 0.11$).