Sleep Apnea and Circadian Extracellular Fluid Change as Independent Factors for Nocturnal Polyuria

Aya Niimi,* Motofumi Suzuki,* Yasuhiro Yamaguchi,† Masaki Ishii, Tetsuya Fujimura, Tohru Nakagawa, Hiroshi Fukuhara, Haruki Kume, Yasuhiko Igawa, Masahiro Akishita and Yukio Homma

From the Departments of Urology (AN, TF, TN, HF, HK, YH), Geriatric Medicine (YY, MI, MA) and Continence Medicine (YI), Graduate School of Medicine, University of Tokyo and Department of Urology, Tokyo Teishin Hospital (MS), Tokyo, Japan

Purpose: We investigated the relationships among nocturnal polyuria, sleep apnea and body fluid volume to elucidate the pathophysiology of nocturia in sleep apnea syndrome.

Materials and Methods: We enrolled 104 consecutive patients who underwent polysomnography for suspected sleep apnea syndrome. Self-assessed symptom questionnaires were administered to evaluate sleep disorder and lower urinary tract symptoms, including nocturia. Voiding frequency and voided volume were recorded using a 24-hour frequency-volume chart. Body fluid composition was estimated in the morning and at night using bioelectric impedance analysis. Frequency-volume chart data were analyzed in 22 patients after continuous positive airway pressure therapy.

Results: Patients with nocturnal polyuria showed a higher apnea-hypopnea index (33.9 vs 24.2, $p = 0.03$) and a larger circadian change in extracellular fluid adjusted to lean body mass (0.22 vs −0.19, $p = 0.019$) than those without nocturnal polyuria. These relations were more evident in patients 65 years old or older than in those 64 years or younger. A multivariate linear regression model showed an independent relationship of nocturnal polyuria with the apnea-hypopnea index and the circadian change in extracellular fluid adjusted to lean body mass ($p = 0.0012$ and 0.022, respectively). Continuous positive airway pressure therapy significantly improved nocturnal polyuria and nocturia only in patients with nocturnal polyuria.

Conclusions: This study identified sleep apnea and the circadian change in extracellular fluid as independent factors for nocturnal polyuria.

Key Words: urinary bladder, polyuria, sleep apnea syndromes, circadian rhythm, body fluids

Abbreviations and Acronyms

AHI = apnea-hypopnea index
ANP = atrial natriuretic peptide
BIA = body impedance analysis
BMI = body mass index
CPAP = continuous positive airway pressure
ECF = extracellular fluid
FVC = frequency-volume chart
I-PSS = International Prostate Symptom Score
LBM = lean body mass
NBCi = Nocturnal Bladder Capacity Index
NP = nocturnal polyuria
NPi = NP index
OABSS = Overactive Bladder Symptom Score
SAS = sleep apnea syndrome
TBF = total body fluid

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* Equal study contribution.
† Correspondence: Department of Geriatric Medicine, Graduate School of Medicine, University of Tokyo, 7-3-1 Hongo, Bunkyo-ku, Tokyo, 113-8655, Japan (telephone: +813 58008652; FAX: +813 58006530; e-mail: yamayasu-tky@umin.ac.jp).

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NOCTURIA is defined as the complaint of having to awaken 1 or more times at night to void.[1] The etiology of nocturia has been described as due to multiple factors, including decreased functional bladder capacity, sleep disorder and NP.[2,3] Of these conditions nocturnal polyuria is presumed to be related to a systematic water imbalance, such as excessive water intake, hypertension during nighttime and edema of the lower limbs.[4]

SAS, which has been suggested as a major cause of nocturia, is characterized by recurrent episodes of airflow cessation during sleep and is most commonly caused by mechanical airway obstruction.[5–7] However, the precise etiological association of SAS and nocturia is under studied. In most previous studies self-reported questionnaires alone were used to estimate nocturia and FVC was rarely adopted to measure urinary volume. Additionally, to our knowledge no study has evaluated body fluid volume in the analysis of the association between SAS and nocturia.

Recently, noninvasive techniques to measure body composition, called BIA have been available. The aim of our study was to elucidate the relationship among SAS, nocturnal polyuria and body fluid volume by polysomnography, FVC and BIA.

MATERIALS AND METHODS

We consecutively enrolled in study 104 patients who were symptomatically suspected of having SAS and who underwent overnight polysomnography at our institution from February 2012 to March 2014. Written informed consent was obtained from all participants under institutional ethics committee approval (No. 38353). Subjective symptoms were evaluated by self-assessment symptom questionnaires such as PSQI (Pittsburgh Sleep Quality Index) for sleep disorder,[8] and I-PSS and OABSS[9] for lower urinary tract symptoms. FVC was recorded during the hospital stay to measure voided urinary volume. Nighttime urinary volume was defined as the volume voided during sleep plus the first volume after arising. The severity of nocturnal polyuria was evaluated by NPi, defined as the proportion of nighttime urinary volume over 24-hour urinary volume. Patients with nocturnal polyuria were classified in the NP group and those without nocturnal polyuria were classified in the nonNP group. Nocturnal polyuria was defined as NPi more than 0.33 in patients 65 years old or older and NPi more than 0.2 in patients 64 years old or younger.[10] NBCi was calculated as the number of nighttime voids − (nocturnal urinary volume/maximum voided volume − 1).[11]

Polysomnography

Polysomnography consisted of pulse oximetry to measure oxygen saturation, and thermistor and nasal air pressure transducer for ventilation to measure the duration and frequency of apnea and hypopnea during sleep. All sleep recordings were visually scored by an experienced rater according to AASM (American Academy of Sleep Medicine) guidelines.[12] The severity of SAS was expressed as AHI, which was the average number of apneas and hypopneas per hour. Apnea was defined as the complete cessation of airflow for more than 10 seconds. Hypopnea was defined as a greater than 50% reduction in flow using nasal pressure, which was associated with arousal and/or 3% desaturation.[13]

Bioelectric Impedance Analysis and FVC Recording

BIA is a noninvasive technique to estimate the amount of fat, skeletal muscle mass and water volume of the body. Water volume was estimated separately for TBF, ECF and intracellular fluid. An edematous state was defined as an ECF-to-TBF ratio (ECF/TBF) greater than 0.4 according to ESPEN (European Society for Clinical Nutrition and Metabolism) guidelines.[14] BMI and LBM were measured to estimate obesity. Analysis was performed with a MC-180 device (TANITA, Tokyo, Japan) at the time of awakening at approximately 7:00 a.m. and before going to bed at approximately 8 p.m. The circadian change in ECF (ΔECF = night ECF − morning ECF) was adjusted by lean body mass and shown as a percent (ΔECF/LBM $\times$ 100).

Patients diagnosed with SAS who started CPAP therapy during sleep were invited to undergo post-CPAP recording of FVC.

Statistical Analysis

Data were analyzed with JMP® Pro, version 11.0.0 and presented as the mean $\pm$ SD. Statistical analysis was performed using the Mann-Whitney U test and the paired t-test to compare continuous variables between groups with $p < 0.05$ considered statistically significant. To determine factors that influenced nocturnal urine production univariate and multivariate linear regression analyses were performed with NPi as the dependent variable. The Wilcoxon signed rank test was used to analyze pre-post changes after CPAP therapy. The correlation of changes among variables was analyzed by the Spearman rank correlation.

RESULTS

A total of 104 consecutive patients were enrolled in this study (table 1). Mean $\pm$ SD age was 63.4 $\pm$ 11.7 years. The prevalence rates of hypertension, diabetes mellitus, cerebral infarction, benign prostatic hyperplasia, chronic heart failure and chronic kidney disease were 43.3%, 36.6%, 9.6%, 29.0%, 6.7% and 19.2%, respectively. We divided patients into 2 groups, including the NP group and the nonNP group, according to NPi. There was no significant difference in background in patients in the 2 groups.

In terms of SAS severity mean AHI was significantly higher in the NP group than in the nonNP group (33.9 vs 24.2, $p = 0.03$), indicating more severe sleep disordered breathing in patients with nocturnal polyuria (table 1). However, there were no