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Voiding Dysfunction

Correlation between Nocturia and Sleep: A Questionnaire Based Analysis

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Purpose: This study evaluated the effectiveness and quality of sleep (QoS) in adult patients with nocturnal lower urinary tract symptoms (LUTS) including nocturia and nocturnal polyuria.

Materials and Methods: A total of 102 patients with nocturia and daytime LUTS were enrolled in this study. All patients completed a questionnaire that included the International Prostate Symptom Score (IPSS), quality of life score (QoL), overactive bladder questionnaire (OABq), and a sleepiness index. The sleepiness index was measured with the Korean Beck Depression Inventory (K-BDI), Insomnia Severity Index (ISI), Epworth Sleepiness Scale (ESS), Berlin Questionnaire (BQ), and the International Restless Legs Syndrome Study Group (IRLSSG). Statistical analyses included the Student's t-test and chi-square test. Differences were considered significant at a p-value of less than 0.05.

Results: Nocturia during sleep was experienced by 68 (66.7%) out of 102 patients. There was no significant association between the nocturia- and the sleep-related scales, but with multiple regression analysis for sex and age, the K-BDI score (p=0.05), IPSS score (p=0.05), and OABq (p=0.02) were significantly higher in patients who woke up to void during sleep. A total of 57 (55.9%) patients diagnosed with overactive bladder with nocturia had severe daytime sleepiness on the ESS questionnaire (p=0.019) and more urgency symptoms on the IPSS questionnaire (p=0.007).

Conclusions: Patients with nocturia had a greater risk of being depressive and felt sleepier during the daytime. LUTS including nocturia and sleep quality closely affected each other. Therefore, clinicians should consider patients' LUTS and sleep problems or QoS as well to provide more satisfying outcomes.

Key Words: *Nocturia; Quality of life; Sleep disorders*

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INTRODUCTION

Lower urinary tract symptoms (LUTS) are known to reduce quality of life (QoL). Nocturnal LUTS such as nocturia (nocturnal frequency) and nocturnal polyuria disrupt the continuity of sleep. This causes poor quality of sleep (QoS), which in turn affects daytime activity and overall QoL. Nocturia also increases fatigue and doubles the risk of falls and injuries at night [1]. Nocturia is common in elderly populations, with a 10-24% rate of incidence [2]; the overall incidence in 18-79-year-old males and females is 37% and 43%, respectively [3].

Treating nocturia is thought to improve QoL, but recent studies have shown that nocturia treatment only lessens nighttime voiding frequency, without changing life qualities [4]. The present study investigated the impact of adult nocturnal LUTS on the QoS and, vice versa, the impact of sleep consistency on LUTS to identify the optimal management strategy for patients with nocturia and sleep disorders.

MATERIALS AND METHODS

All study protocols were reviewed and approved by the Institutional Review Board of the Clinical Research Center of the author's hospital.

In this prospective, randomized study, 102 adults aged 23 to 84 years with symptoms of nocturia and daytime LUTS were enrolled from January to June 2009. Patient history, physical examination, a 3-day frequency volume chart, International Prostate Symptom Score (IPSS), quality-of-life score (QoL), overactive bladder questionnaire (OABq), and uroflowmetry with residual urine check by ultrasonography were completed for all participants.

Patients who had been receiving treatment for LUTS for more than 3 months and with any type of sleep disturbances were enrolled. Patients treated with centrally acting drugs that may have affected LUTS or sleep patterns within the previous 1 month were excluded. Patients with polyuria due to external causes were also excluded.

In this study, nocturia was defined as waking to void more than once per night. Every patient was asked to complete a 3-day frequency-volume (FV) chart. With the self-reported FV chart, each patient was interviewed about his or her nighttime voiding habits and sleep patterns or sleep quality. According to these results, the patients were divided into 2 groups: those who woke to void at night (nocturia) comprised the 'true nocturia' group, and those who unnecessarily voided as a consequence of having been awakened comprised the 'pseudo nocturia' group.

Overactive bladder was defined as urinary frequency and urgency as determined according to International Continence Society criteria by history taking of voiding symptoms and voiding pattern from a 3-day FV chart [5].

Sleep disruption was investigated by one medical doctor, patient interviews, and sleep-related questionnaires. Sleep questionnaires consisted of questions about basic demographic data (age, sex, body weight, height, and marriage and employment status), consumption of alcohol, smoking, caffeine intake, medical disease (to identify the presence of any medications that might affect nighttime urine volume), cardiovascular disease, pulmonary disease, neurologic disease, and diabetes mellitus.

Questionnaires for the detection and analysis of sleep problems were all translated into Korean; of these, the Korean Beck's Depression Inventory (K-BDI) had been previously validated. The questionnaires included the Epworth Sleepiness Scale (ESS) for daytime sleepiness (significantly severe daytime sleepiness: ESS total score $\geq$ 10) [6]; the K-BDI for mood disorder screening (in men, mild depression: 16-19, moderate depression: 20-23, severe depression $\geq$ 24; in women, mild depression: 17-20, moderate depression: 21-24, severe depression $\geq$ 25) [7]; the Berlin Questionnaire (BQ) for sleep apnea (high risk group score= 1, low risk group score=0) [8]; the Insomnia Severity Index (ISI) for measuring the intensity of insomnia (normal: 0-7 points, subthreshold insomnia: 8-14 points, moderate insomnia: 15-21 points, severe insomnia: $>$ 22 points,) [9]; and the International Restless Legs Syndrome Study Group (IRLSSG) for restless leg syndrome (mild: 1-10 points, moderate: 11-20 points, severe: 21-30 points, very severe: 31-40 points) [10].

All scores from the LUTS and sleep questionnaires were collected and analyzed with SAS ver. 8.2 (SAS Institute Inc., Cary, NC, USA) to determine the correlation between LUTS and sleep-associated QoL by using the Student's t-test, chi-square test, and multiple regression analysis. Statistical differences were considered significant at a p-value less than 0.05.

RESULTS

The patient cohort included 44 men (43.1%) and 58 women (56.9%). The mean age of the patients was 56.89±14.56 years (men, 63.36±11.13 [24-81] years; women, 51.98±15.02 [23-84] years). Patients complaining of LUTS included 85 out of 102 (83.4%) patients. Within the LUTS group, nocturia was present in 28 (27.5%) patients, and overactive bladder (OAB) was present in 57 (55.9%) patients.

The patients' mean body mass index (BMI) was 23.57± 3.45 kg/m^2. A total of 74 of the 102 patients (72.5%) regularly consumed caffeine (Table 1). Forty patients (39.22%) had comorbidities, including 23 with hypertension, 7 with diabetes, 5 with hypertension and diabetes, 2 with angina, 1 with heart failure, 1 with asthma, and 1 with spinal stenosis. Other patient characteristics that may have affected sleep quality or LUTS are shown in Table 1.

Patients' mean voiding volume was 213.39±72.86 ml, mean maximal flow rate (Qmax) was 18.74±20.08 ml/s, and mean postvoid residual urine volume was 27.33±47.61 ml.

LUTS scores included the mean total IPSS score (14.94± 8.34) and the mean QoL score (3.99±1.39). Sleep problem scores included the mean K-BDI (7.26±3.29), ISI (7.93± 6.84), ESS (5.69±4.65), and IRLSSG (2.48±5.97). In addition, the percentage of patients at high risk on the BQ was 6.9%.

TABLE 1. Patients' characteristics

	Total No. of patients (%)	Female	Male
n	102	58	44
Age (yr)	56.89±14.56	51.98±15.02	63.36±11.13
BMI	23.57±3.45	23.45±3.99	23.76±2.43
Alcohol	42 (41.18)	23	19
Smoking	14 (13.73)	4	10
Caffeine	65 (63.73)	38	27
Comorbidity	40 (39.22)	23	17
Married	85 (83.33)	50	35
Employed	34 (33.33)	16	18

BMI: body mass index, Alcohol: drink more than once per week, Caffeine: drink coffee or caffeine contained in tea more than once per day, Comorbidity: diabetes mellitus, hypertension, cardiac disease, pulmonary disease, neurologic disease

TABLE 2. Differences between sleep-related indices and nocturia

Sleep indices	Nocturia		p-value
	True	Pseudo	
Total No. of patients (n=102)	68	34	
ESS	5.87±5.71	4.97±4.99	0.342[a]
K-BDI	15.41±14.49	10.73±12.67	0.052[b]
BQ (high-risk n)[c]	7	5	0.517[b]
ISI	7.72±8.05	8.22±9.43	0.734[a]
IRSSG	2.07±6.0	2.67±4.85	0.783[b]
OAB No. of patients (n=50)	38	12	
ESS	6.6±5.81	5.58±2.61	0.019[a]
K-BDI	17.1±14.1	11.67±11	0.122[b]
BQ (high-risk n)[c]	3	2	0.619[b]
ISI	6.76±4.64	6.25±6.27	0.473[a]
IRSSG	2.18±5.89	3.33±5.66	1[b]

True nocturia: waking up to void at night, False nocturia: unnecessary voiding as a consequence of being awakened, ESS: Epworth Sleepiness Scale, K-BDI: Korean Beck Depression Inventory, BQ: Berlin Questionnaire, ISI: Insomnia Severity Index, IRLSSG: International Restless Legs Syndrome Study Group, [a]: Student's t-test, [b]: chi-square test, [c]: more than 2 categories positive in 3 categories defined as high-risk group

A total of 68 of the 102 patients (66.7%) complained of waking up at night to void (true nocturia); however, there was no significant correlation between 'waking up at night to void' and 'the daytime sleepiness scale' (Table 2).

To analyze the correlation between nighttime frequency (true nocturia) and other voiding symptom scores, the IPSS was divided into the sum of 7 storage and voiding symptom scores: (Q2 [frequency], Q4 [urgency], and Q7 [nocturia]) and (Q1 [emptying], Q3 [intermittency], Q5 [weak stream], and Q6 [hesitancy]) (Table 3). Question number 5 (weak stream) showed a statistically significant correlation between LUTS and the presence of bladder irritation during sleep (p=0.009). The QoL score showed no significant correlation (p=0.076) (Table 3).

The scores for each question and the total OABq score were analyzed. Question number 5 (nighttime urination) (p=0.004), question number 6 (waking up at night because of urination) (p=0.01), and the total OABq score (p=0.013) showed a statistically significant correlation (t-test) (Table 3).

The K-BDI score was significantly higher in patients who woke up to void during sleep (p=0.05). In the true nocturia group, the mean total IPSS scores (p=0.05) and the mean total OABq scores (p=0.02) were significantly higher after adjusting for age and sex by multiple regression analysis (Table 4). However, when only OAB patients were analyzed, there was no significant correlation (Table 4).

TABLE 3. Differences between voiding symptom scores and nocturia

Questions	Nocturia		p-value
	True (n=68)	Pseudo (n=34)	
IPSS			
IQ1 (emptying)	2.28±1.89	1.85±1.95	0.29[a]
Q2 (frequency)	2.86±1.63	2.42±1.54	0.2[a]
Q3 (intermittency)	2.07±1.66	1.79±1.75	0.42[a]
Q4 (urgency)	2.19±1.76	1.67±1.67	0.16[a]
Q5 (weak stream)	2.81±1.57	1.88±1.82	0.009[a]
Q6 (hesitancy)	1.62±1.63	1.33±1.63	0.4[a]
Q7 (nocturia)	2.22±1.42	1.73±1.51	0.11[a]
Storage symptom (Q2, Q4, Q7)	7.26±3.85	5.82±3.92	0.081[b]
Voiding symptom (Q1, Q3, Q5, Q6)	8.78±5.32	6.85±5.57	0.093[b]
IPSS total score	16.03±8.12	12.67±8.46	0.056[b]
QoL	4.18±1.22	3.66±1.6	0.076[b]
OABq			
Q1 (daytime frequency)	1.91±1.58	1.48±1.54	0.2[a]
Q2 (uncomfortable urge)	1.81±1.47	1.3±1.42	0.1[a]
Q3 (sudden urge)	1.24±1.55	0.85±1.35	0.21[a]
Q4 (accidental loss of urine)	1.2±1.56	0.7±1.18	0.1[a]
Q5 (nighttime urination)	2.62±1.62	1.61±1.6	0.004[a]
Q6 (waking up at night for urination)	2.62±1.65	1.73±1.52	0.01[a]
Q7 (uncontrollable urge)	1.67±1.64	1.27±1.4	0.23[a]
Q8 (urine loss c strong desire to urination)	1.23±1.64	0.76±1.32	0.15[a]
OABq total score	14.3±8.72	9.7±8.32	0.013[b]

True nocturia: waking up to void at night, False nocturia: unnecessary voiding as a consequence of being awakened, IPSS: International Prostate Symptom Score, QoL: quality of life score, OABq: Overactive Bladder questionnaire, [a]: chi-square test, [b]: Student's t-test

TABLE 4. Multiple regression analysis adjusted for patients' age and sex

	β	p-value
Total No. of patients (n=102)		
Sleep indices		
ESS	0.79	0.4
K-BDI	4.72	0.05
ISI	−0.64	0.66
Voiding scales		
Storage sx.	1.4	0.09
Voiding sx.	2.07	0.08
IPSS total score	3.45	0.05
QoL	0.44	0.13
OABq total score	4.25	0.02
OAB No. of patients (n=50)		
Sleep indices		
ESS	0.59	0.76
K-BDI	6.64	0.2
ISI	1.16	0.58
Voiding scales		
Storage sx.	2.07	0.17
Voiding sx.	2.38	0.25
IPSS total score	4.45	0.18
QoL	0.42	0.39
OABq total score	5.43	0.14

ESS: Epworth Sleepiness Scale, K-BDI: Korean Beck Depression Inventory, ISI: Insomnia Severity Index, Storage sx.: sum of IPSS questions 2, 4, and 7, Voiding sx.: sum of IPSS questions 1, 3, 5, and 6, IPSS: International Prostate Symptom Score, QoL: quality of life score, OABq: Overactive Bladder questionnaire

The correlations between nocturia and various sleep-related scales were analyzed in patients diagnosed with OAB. Patients with OAB with nocturia or nighttime frequency during sleep more frequently reported "severe daytime sleepiness" on the ESS questionnaire (p=0.019); however, these patients did not show any significant correlation with other sleep problem scales (Table 2).

The correlation between each LUTS questionnaire and the presence or absence of voiding during sleep (true or pseudo nocturia) was compared and analyzed. In the IPSS score, the question regarding urgency (Q4) was significantly correlated with patients with true nocturia (p=0.007); however, there was no significant correlation between nocturia and the QoL IPSS score or the OABq scores (Table 5).

DISCUSSION

Over 72% of the elderly wake up more than once during sleep to void, and 24% of them are awakened more than 3 times per night [11,12]. Nocturia diminishes the general QoL, QoS, daytime functioning, morbidity, and mortality [12]. Nocturia can be associated with numerous urological pathologies such as LUTS-benign prostatic hyperplasia (BPH), OAB, neurogenic voiding dysfunction, bladder cancer, and so on. It can also be associated with nonurological diseases and conditions such as congestive heart failure, diabetes mellitus, diabetes insipidus, hypoalbuminemia, sleep apnea syndrome, multiple sclerosis, depression,

TABLE 5. Differences between voiding symptom scores and nocturia in OAB patients

Questions	Nocturia		p-value
	True (n=38)	Pseudo (n=12)	
IPSS			
Q1 (emptying)	2.58±1.85	1.33±1.78	0.809[a]
Q2 (frequency)	2.86±1.63	2.42±1.54	0.269[a]
Q3 (intermittency)	2.07±1.66	1.79±1.75	0.903[a]
Q4 (urgency)	2.19±1.76	1.67±1.67	0.007[a]
Q5 (weak stream)	2.81±1.56	1.88±1.81	0.414[a]
Q6 (hesitancy)	1.62±1.63	1.33±1.63	0.622[a]
Q7 (nocturia)	2.21±1.42	1.73±1.5	0.341[a]
Storage sx. (Q2, Q4, Q7)	8.05±3.3	6.33±4.75	0.237[b]
Voiding sx. (Q1, Q3, Q5, Q6)	7.45±5.57	5.83±5.31	0.425[b]
IPSS total score	15.5±8.08	12.17±9.41	0.365[b]
QoL	4.37±1.01	4.08±1.62	0.592[b]
OABq			
Q1 (daytime frequency)	1.91±1.58	1.48±1.54	0.471[a]
Q2 (uncomfortable urge)	1.81±1.47	1.3±1.42	0.149[a]
Q3 (sudden urge)	1.24±1.55	0.85±1.35	0.654[a]
Q4 (accidental loss of urine)	1.2±1.56	0.7±1.18	0.728[a]
Q5 (nighttime urination)	2.62±1.62	1.61±1.6	0.268[a]
Q6 (waking up at night for urination)	2.62±1.65	1.73±1.52	0.223[a]
Q7 (uncontrollable urge)	1.67±1.64	1.27±1.4	0.646[a]
Q8 (urine loss c strong desire to urination)	1.23±1.64	0.76±1.32	0.345[a]
OABq total score	16.7±8.93	12.42±10.34	0.225[b]

True nocturia: waking up to void at night, False nocturia: unnecessary voiding as a consequence of being awakened, IPSS: International Prostate Symptom Score, QoL: quality of life score, OABq: Overactive Bladder questionnaire, [a]: chi-square test, [b]: Student's t-test

chronic pain, pruritus, and inadequate fluid intake [13]. Poor QoS due to nocturia results in daytime fatigue, cognitive impairment, mood alterations, increasing disease morbidity, poor productivity, and a higher risk of traffic accidents due to lack of sleep [14].

Several reports have shown that some types of sleep disorders are associated with LUTS [15-19]. Yoshimura et al studied 6,000 patients aged 41-70 years old with a questionnaire about nocturnal voiding/nocturia and sleep disorders [16]. They concluded that insomnia and obstructive sleep apnea syndrome were significantly correlated with nighttime voiding. Periodic limbic movement disorder was also correlated with bothersome nighttime voiding. In contrast, restless leg syndrome was not significantly correlated with nighttime voiding [16].

Clinically, many people suffer with either LUTS or sleep problems at night; however, without careful inspection, it is not easy to differentiate which one is primary: poor sleep quality due to nighttime LUTS or additional, unnecessary voiding due to interrupted sleep at night. Although nocturia and nocturnal polyuria are more common in elderly patients, the aforementioned situations may also occur frequently among younger populations. Our study population encompassed a wide age range (from 20s to 80s), because patient selection was based on symptomatic nighttime voiding for any reason, even with proper treatment of LUTS.

Disruptions of the sleep cycle for any reason can reduce QoL. Several recent studies have reported a correlation between LUTS and QoL, supporting the correlation between nocturia, sleep disruptions, and QoL [14,15]. Nocturia was more strongly correlated, resulting in decreased daytime performance and general well-being.

There were no significant correlations between patient responses on the IPSS or OABq and the presence of nocturia, except for the IPSS urgency question (Q4). We suggest that, because our patients were undergoing treatment for their LUTS (either OAB or LUTS-BPH), their treatment may have affected their responses on the questionnaires.

We analyzed the data as a whole and with the data from OAB patients with or without nocturia excluded and found interesting results. In general, QoL and total IPSS and OABq symptoms scores were significantly correlated with the presence of nocturia, although IPSS, QoL, and total score showed borderline significance (IPSS QoL p=0.056; IPSS total p=0.076; OABq total p=0.013). However, when OAB patients were excluded from the analysis, the scores from both LUTS questionnaires showed significant differences. These findings support the hypothesis that some nocturia patients with low QoL may be affected more by masked or ignored sleep problems.

Scores on IPSS question 7 (Q7, about nocturia) showed no difference between the true and pseudo nocturia groups. However, this question was based on the patients' subjective symptoms but did not account for the voiding diary; any patient who was suffering from frequent nighttime voiding produced a high score.

Multiple regression analysis showed a significant correlation between true nocturia and K-BDI (p=0.05), IPSS total score (p=0.02), and OABq total score (p=0.05). These data support the hypothesis that nocturia is a significant factor affecting subjective symptom severity and the severity of LUTS and daytime sleepiness and that it further affects mental health. We can easily presume that depressive people lack satisfaction with their QoL.

Irwin et al reported that the adverse effect of nocturia on QoL is related to sleep disorders [17]. Nocturia is the major cause of sleep disorders for those over age 50 [18]. Not only awakening from sleep to void at night but also the antimuscarinics prescribed to treat nocturia, by their action on the central nervous system, may disrupt sleep [15,19].

We investigated the correlation between sleep disturbance and nocturia with the ESS for daytime sleepiness, K-BDI for mood disorders, BQ for sleep apnea syndrome, ISI for insomnia, and IRLSSG for restless leg syndrome. In OAB patients, daytime sleepiness was significantly more severe with nocturia. Depression scores were significantly higher in the LUTS group with true nocturia after adjustment for age and sex. They also showed significantly decreased QoL scores. The daytime sleepiness scale was also significantly affected by nocturia.

The result of this study support the hypothesis that nocturia significantly affects QoL in LUTS patients. Although poor sleep quality and sleep disorders might also negatively affect QoL, our group of LUTS patients showed significant differences between waking up to void and voiding because they were unable to sustain sleep. In other words, patients with LUTS combined with bothersome nocturia reported more negatively on their daily life or mental health than did patients without those symptoms. Some patients with simple sleep disruption can be relatively easily relived from their sleep problem with proper medications. Therefore, if they have concurrent nighttime frequency caused by a fragmented sleep pattern, they would not consider nocturia as a significant problem after proper treatment of the sleep problem. However, the scenario is different in LUTS with nocturia patients without an underlying sleep problem. If their LUTS are not controlled enough even in nighttime, they also have disruption in sleep quality, leading to poor general condition and increasing autonomous tone. These would also contribute to aggravating LUTS and life quality. Daytime sleepiness leads to poor nighttime sleep quality, and daily activities become more risky, especially in the elderly population.

There are some discrepancies between the whole LUTS population and the same population with OAB patients excluded. At first, we hypothesized that nocturia as a component of OAB might appear as nocturnal frequency with decreased nocturnal bladder volume. Therefore, waking up often to void will lead to disruption of sleep. Because we excluded only patients with nocturnal polyuria from external origins such as heavy drinking and diuretics usage, some LUTS patients without OAB might have nocturnal polyuria. Because all of the patients were undergoing treatment for LUTS for more than 3 months, we think it

is possible that there was no difference between the true and pseudo nocturia groups' IPSS or OABq scores. Only the IPSS urgency score differed significantly between the true and pseudo nocturia groups. This is also likely to be the effect of treatment and the fact that the IPSS questionnaire was relatively less specific than the OABq.

This study clearly had some limitations. The sleep-related questionnaires (ESS, BQ, ISI, IRLSSG) we used were simply translated into Korean without proper validation. However, the Korean versions of the questionnaires we used are widely being used in the clinical setting.

This study supports the hypothesis that LUTS, particularly nocturia, and sleep closely affect each other. Clinically, it is common to consider nocturnal frequency as the result of sleep disorders or insomnia. In addition, it is particularly common among the elderly. However, clinicians should be certain to differentiate the main cause of poor sleep quality. Tailored management of LUTS and sleep disorders that improves the QoS and corrects voiding symptoms will provide successful treatment results and improve QoL.

CONCLUSIONS

LUTS including nocturia and sleep quality closely affect each other. Patients with nocturia had a greater risk of being depressive and felt sleepier during the daytime. Therefore, clinicians should consider their patients' LUTS and sleep problems or QoS as well to provide more satisfying outcomes.

Conflicts of Interest

The authors have nothing to disclose.

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