Sleep Analysis of Patients With Nocturia and Benign Prostatic Obstruction

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OBJECTIVE
To analyze the timing of nocturia during sleep and its effect on sleep quality using the polysomnography (PSG) findings from patients with benign prostatic obstruction.

METHODS
From August 2009 to August 2010, 20 patients diagnosed with benign prostatic obstruction were enrolled in the present study. The sleep evaluation was performed by PSG. The Epworth index was used to evaluate the sleepiness of the patients. The effect of nocturia on sleep quality is evaluated by sleep efficacy, total sleep time, and rapid eye movement sleep duration, calculated from the hypnograms derived from the polysomnograms.

RESULTS
The mean age, total International Prostate Symptom Score, nocturia frequency on International Prostate Symptom Score, and frequency of nocturia recorded during PSG was 60.4 ± 8.5 years (range 44-74), 19.3 ± 4.9 (range 10-28), 3.5 ± 1.05 (range 2-5), and 1.35 ± 1.2 (range 0-4), respectively. In 6 patients (30%), the Epworth sleepiness score was pathologic (score >8). Nocturia correlated positively with increased daytime sleepiness, however it did not correlate with sleep efficacy or total sleep time. These parameters were affected by the apnea-hypopnea index, the major determinant of obstructive sleep apnea. Of the 20 patients, 14 (70%) experienced nocturia during PSG, and in these patients, we recorded 23 nocturia episodes that mostly occurred in the superficial sleep stage (16 [70%] of 23). Only 7 nocturia episodes (30%) occurred in the deep sleep stage. The sleep quality of patients with deep sleep nocturia did not differ from that of patients with superficial sleep nocturia.

CONCLUSION
The results of our study have shown that nocturia predominantly occurs during the superficial sleep or rapid eye movement stage and is related to increased daytime sleepiness in patients with benign prostatic obstruction. The timing and frequency of nocturia had no significant affect on sleep quality; however, the presence of obstructive sleep apnea negatively interfered with these parameters.

The International Continence Society has defined nocturia as “the complaint the individual has to wake at night one or more times to void.”1 The prevalence of nocturia in men <30 years is 3.4%; the incidence increases ≥32.4% among men >60 years old.2 The etiology of nocturia is multifactorial. It can result from polyuria (eg, excessive fluid intake, diabetes mellitus, diabetes insipidus), nocturnal polyuria (eg, impaired nocturnal arginine vasopressin, obstructive sleep apnea, congestive heart failure), a decreased (nocturnal) bladder capacity (benign prostatic hyperplasia with detrusor overactivity and/or postvoid residual urine volume, detrusor overactivity alone), or a combination of these factors.3 Nocturia is 1 of the major symptoms suggestive of benign prostatic obstruction (BPO).4 Together with other storage symptoms, nocturia causes more bother to the patient with lower urinary tract symptoms/BPO.5

It is known that nocturia is related to poor sleep and that an increased frequency of nocturia has a negative effect on sleep quality and overall health-related quality of life.6-8 The timing of nocturia is important with regard to its effect on sleep architecture. The amount of slow wave sleep (non-rapid eye movement [REM] or deep sleep) has special importance, because it is related to physical rest, bolstering of the immune system, and, therefore, the restorative function of sleep.9 It has been shown that deep sleep occurs during the first hours of the night.9 The hours of undisturbed sleep (HUS) refers to the period from falling asleep until waking up to urinate.10,11

To objectively analyze the effect of nocturia on sleep quality, we used polysomnography (PSG)—the reference
standard of objective sleep assessment. The main objectives of the present study were to demonstrate the exact timing of nocturia in the sleep architecture of patients with BPO; to evaluate the effect of nocturia occurring in different phases of sleep and the sleep quality of patients with BPO; and to identify any other factors related to nocturia from the measurements derived from the PSG.

To our knowledge, the present study is the first English published report to evaluate the sleep characteristics of nocturia in patients with BPO in the sleep laboratory.

**MATERIAL AND METHODS**

After approval of the study design by the local ethics committee, patient enrollment began in August 2009 and lasted until August 2010. A total of 20 patients volunteered to participate in the study, and these patients provided written consent. All patients had moderate to severe lower urinary tract symptoms and nocturia frequency of ≥2/night. All patients were diagnosed with symptomatic BPO were candidates for treatment.

**Diagnostic Tests for BPO**

After a careful medical history and lower urinary tract symptom assessment with the International Prostatic Symptom Score (IPSS), a detailed physical examination, including the digital rectal examination, was performed. Samples for urinalysis, blood urea nitrogen, serum creatinine and electrolytes, and serum prostate-specific antigen were obtained from the patients. The kidneys, bladder, and prostate were examined using transabdominal ultrasonography. The postvoid urinary volume was determined using ultrasonography performed after uroflowmetry.

The patients were considered candidates for treatment of BPO if they had an IPSS >12 and/or a diminished average urine flow (<10 mL/s) and/or an increased postvoid residual urine volume (>50 mL). Because it was not recommended for routine clinical workup for patients with symptoms suggestive of BPO, invasive tests, such as pressure flow urodynamics, were not performed as a part of the study protocol.

The patient withdrawal criteria were as follows:

- Previous surgery of the lower urinary tract
- Diagnosis of overactive bladder symptoms, urethral stricture, chronic prostatitis, or urinary tract infection
- Presence of any malignancy
- Previous evaluation for the presence of obstructive sleep apnea syndrome (OSAS) or treatment of OSAS
- Insomnia or any type of sleeping problems other than nocturia
- Neurologic conditions, such as Parkinson’s disease, multiple sclerosis, spinal cord injury
- Use of medications, such as diuretics, anticholinergics, tricyclic antidepressants, serotonin reuptake inhibitors, or any drug interfering with sleep
- Medical history of diabetes mellitus, diabetes insipidus, congestive heart failure, chronic obstructive lung disease, bronchial asthma, coronary artery disease, major depression, or any psychological or physical condition that might interfere with sleep activity or make it impossible for the patient to participate in the study

The patients who volunteered and were eligible for the study underwent additional evaluations with the Epworth scale and PSG.

**Epworth Sleepiness Scale**

The daytime sleepiness of the patients was evaluated using the Epworth Sleepiness Scale (Fig. 1), a brief questionnaire that subjectively measures an individual’s likelihood of falling asleep in real-life situations, such as sitting, reading, watching television, driving, and so forth. The score range was 0 to 24, with greater scores correlating with increased sleepiness. When used as a screening tool, a score >8 indicates the need for a consultation from a sleep specialist.

**Polysomnography**

To identify the effect of nocturia on sleep architecture, the patients underwent a single overnight PSG study. During PSG, recordings of the central and occipital electroencephalography, submental electromyography, bilateral electrooculogram, airflow, patient position, bilateral anterior tibial electromyography, electrocardiography, respiratory efforts, pulse oximeter, and video monitoring of the patients were also obtained. Patients entered the test room at 8:00 PM. The lights were turned off at 10:00 PM and recordings begun. Polysomnograms were performed and reported by 1 of us (S.A.), a certified specialist. PSG is also routinely used to objectively diagnose OSAS. OSAS is the repetitive episodes of complete or partial upper airway obstruction resulting in apnea during deep sleep. Apnea will result in disruption of sleep and decreases in blood oxygen levels. During an episode of apnea, the patient either wakes up completely or passes from deep sleep to shallow sleep. Hypopnea is a decrease in breathing that is not as severe as apnea. It is also associated with the disruption of sleep and a decrease in oxygen saturation. The apnea-hypopnea index (AHI) is used to measure the severity of sleep apnea and is calculated by dividing the number of apnea episodes and hypopnea episodes by the hours of sleep.

The effect of nocturia on sleep quality is measured by determining the sleep efficacy (SE; the proportion of actual time spent in sleep to the total time spent in bed), total sleep time (TST), and REM sleep duration on the hypnograms derived from the single overnight PSG. We assessed the relationship between the fre-
BMI was 23.6 kg/m². The BMI of 12 patients was within normal limits (18.5-25 kg/m²). Of the remaining 8 patients, 7 were overweight with a BMI of 25-29.9 kg/m² and 1 who was obese, with a BMI of 31.4 kg/m². We therefore analyzed this issue.

In our study population, all the patients reported nocturia. The HUS correlated significantly with the actual nocturia frequency recorded during PSG but not with the IPSS item assessing nocturia. The HUS did not correlate with the SE, TST, or REM sleep time.

However, the Epworth sleepiness index did not correlate with the nocturia episodes recorded during PSG, TST, SE, HUS, or REM sleep duration.

**RESULTS**

This was a relatively small-size study with limited statistical power; therefore, the results should be interpreted accordingly.

The mean patient age was 60.4 ± 8.5 years (range 44-74). Most patients had moderate to severe lower urinary tract symptoms. The mean IPSSs of the patients are listed in Table 1. Using the IPSS questionnaire, the patients reported their nocturia frequency, which varied from 2 to 5 episodes per night (mean 3.5 ± 1.05). However, the actual nocturia frequency recorded during PSG was 0-4 (mean 1.35 ± 1.2). The difference between the reported and actual nocturia was significant (P < .05). Of the 20 patients, 11 reported that nocturia was the most bothersome symptom for them, and 9 reported that incomplete emptying caused the most bother.

The BMI, uroflowmetry, and laboratory and ultrasound findings of the patients are listed in Table 2. The median BMI was 23.6 kg/m². The BMI of 12 patients was within normal limits (18.5-25 kg/m²). Of the remaining 8 patients, 7 were overweight with a BMI of 25-29.9 kg/m² and 1 who was obese, with a BMI of 31.4 kg/m². We recorded no difference between sleep quality and nocturia frequency for the patients according to the BMI.

**Epworth Results**

The mean Epworth score of the patients was 6.25 ± 4.1 (range 0-15). The score of 14 patients was <8 (within normal limits). However, the score of 6 patients was >8, demonstrating increased sleepiness.

The Epworth score correlated positively with reported nocturia frequency, and this correlation was significant (Pearson correlation 0.472, P = .03).

However, nocturia frequency, both reported by the patient and recorded during PSG, did not correlate with SE, TST, or REM sleep duration.

**Nocturia Timing**

Of the 20 patients, 14 (70%) had nocturia during PSG. In these patients, we recorded 23 nocturia episodes. These mostly occurred during superficial or REM sleep stage (16 [70%] of 23). Only 7 nocturia episodes (30%) occurred in the deep sleep stage. The SE, TST, and Epworth sleepiness score of the patients with nocturia during deep sleep did not differ from those of the patients with nocturia during superficial or REM sleep.

**COMMENT**

Disturbed sleep due to nocturia in patients with BPO is a bothersome condition and has a major effect on the patients' general well being and health-related quality of life. Whatever the cause, it is obvious that waking up for urination has detrimental effects on one's sleep quality. However, this conclusion was derived from studies in which sleep quality was assessed by patient-completed subjective inventories or sleep diaries. Sleep logs and diaries could be inaccurate owing to their subjective nature, because they can overestimate sleep onset and latency and underestimate the sleep time. Moreover, in recent years, it has been speculated that not only the frequency, but also the timing of nocturia, is an important determinant of sleep quality. It has been argued that nocturia occurring in the first 3-4 hours of sleep and/or in the deep sleep phase has a worse effect on SE by reducing the hours of undisturbed sleep and shortening the time spent in deep sleep. However, to date, no study has objectively analyzed this issue.

The question of whether patients with nocturia and BPO really sleep as badly as they report can only be answered if we test the situation.

In our study population, all the patients reported nocturia on the IPSS; however, only 14 of 20 patients demonstrated...
nocturia on the PSG. Moreover, those 14 patients with nocturia during PSG demonstrated significantly fewer nocturia episodes than they report on IPSS (1.35 ± 1.2 vs 3.5 ± 1.05, P < .05).

One of the interesting findings of our study was the demonstration of another factor interfering with the sleep quality of patients with BPO—the presence of OSAS. It is characterized by repetitive episodes of upper airway obstruction occurring during deep sleep, and it is usually associated with a reduction in the blood oxygen saturation. Apnea will result in disruption of sleep and a decrease in blood oxygen levels. During an episode of apnea, the patient either wakes up completely or passes from deep sleep to shallow sleep. Hypopnea is a decrease in breathing that is not as severe as apnea; however, it is also associated with a disruption of sleep and a decrease in oxygen saturation. The AHI is used to measure the severity of sleep apnea and is calculated by dividing the number of apnea and hypopnea episodes by the hours of sleep.

In our study, more than one half of the patients had varying degrees of obstructive sleep apnea according to the AHI measurements. We found that AHI had a strong relationship with objective sleep quality in our patients with nocturia and BPO. The TST, SE, and REM sleep duration correlated significantly with the AHI. However, nocturia frequency, both reported by the patient and recorded during PSG, did not correlate with the SE, TST, and REM sleep duration. Hence, in our study, we failed to demonstrate a correlation between nocturia frequency and objective sleep quality. However, we found that AHI significantly influenced these parameters. When we further compared the SE, TST, and REM sleep duration of the patients with and without OSAS, we found a slightly better SE in the patients without OSAS (77% vs 67%, P = .058).

The timing of nocturia in the sleep of a patient with nocturia and BPO was the main subject of investigation in the present study. The timing of nocturia during sleep has a significant effect on the sleep architecture. Recently, the concept of HUS has been introduced as a new potential method to measure the effect of nocturia on sleep quality. It has been shown that sleep deep (slow wave sleep) predominates in the first hours of the night. This period is then followed by shallow sleep and REM sleep episodes, which are less physically restorative. Therefore, waking up in the first few hours of sleep or waking up from a deep sleep stage will result in daytime fatigue and sleepiness. Is this the case for a patient with nocturia and BPO? In the present study, examining the timing of nocturia in the architecture of sleep has given us the possibility of objectively assessing this issue.

We found that most of the nocturia episodes recorded occurred in the superficial or REM sleep phase, not in the deep sleep stages (Fig. 2). Moreover, the characteristics of the patients experiencing nocturia in deep sleep do not differ from those of the patients with nocturia in superficial sleep as determined by the SE, REM sleep time, and TST.

Our result showed that, although HUS correlated significantly with the observed nocturia episodes (but not the reported episodes), it had no effect on sleep quality. Our data failed to demonstrate any correlation between HUS and the SE, TST and REM sleep time.

The nocturnal bladder capacity index (NBCi), derived from the voiding diary, is a quantitative method of comparing the nocturnal bladder capacity with the 24-hour bladder capacity. The NBCi has been shown to be useful in comparing multifactorial etiologies of nocturia. In their recent study, Burton et al aimed to obtain the reference values of NBCi from an asymptomatic population. They suggested that an unrounded NBCi of 1.3 can be considered a cutoff point above which decreased nocturnal bladder capacity should be investigated as an etiologic contributor to nocturia. Although the NBCi is useful in identifying the contribution of diminished nocturnal capacity to nocturia, it does not help to clarify the underlying conditions leading to a low nocturnal bladder capacity. The investigators commented that the finding of a low bladder capacity should lead the physician to investigate the underlying reasons the patient is awakened to go to the bathroom for volumes lower than those prompting urination in daytime when the patient is awake. In the present study, our findings suggest that, together with BPO, OSAS could be such an underlying condition, resulting in nocturia.

Owing to age, anatomic and physiologic factors, or other clinical conditions, patients with BPO might also be susceptible to having OSAS. Patients with OSAS will have apnea in deep sleep, which will result in increased sleepiness and worsened quality of life. However, patients would not attribute this situation to their apnea, of which they are unaware, rather they will tend to blame their nocturia for their disturbed sleep, because they can precisely identify a nocturia episode better than they can identify apnea.

While interpreting our results, we were also aware of the limitations of our study. First, we had a limited number of
patients. PSG is an expensive method of sleep evaluation. Its interpretation is time-consuming, and patients sometimes find this test disturbing and burdensome. Because of technical and institutional limitations, we were able to perform only a single overnight PSG, and this might not reflect the patients’ general sleeping habits. The major drawback of our study was that it lacked a control group. We are also aware that the significance of our results should be validated with data derived from future randomized controlled studies with larger numbers of patients. However, rather than establishing solid statements, we hope that the preliminary results of our study would inspire investigators to handle the dilemma of nocturia differently.

A valuable study design should integrate the PSG and ambulatory urodynamic findings for patients with BPO to precisely evaluate the interactions between the bladder and central nervous system during sleep. In the present study, we were unable to manage this owing to financial and technical limitations. In a recent study, patients with nocturia and overactive bladder were evaluated with both PSG and ambulatory overnight urodynamics. The results of that study, although with a limited number of patients, indicated that nocturnal detrusor overactivity is not associated with sleep disturbances and does not occur before nocturia events in patients without an overactive bladder.17

In addition to nocturnal polyuria, nocturnal detrusor overactivity, or diminished bladder capacity, a more complex mechanism involving the central nervous system, autonomic nervous system, and respiratory system probably underlies the pathophysiology of nocturia. Therefore, treating nocturia as a symptom of the lower urinary tract will underestimate the underwater portion of an iceberg. We believe that additional studies focusing on the nature of nocturia will be published in the near future.

CONCLUSIONS
The objective evaluation of sleep characteristics of patients with BPO using PSG has yielded following conclusions. Nocturia predominantly occurs during superficial sleep or REM stage and it is related to increased daytime sleepiness in patients with BPO. Also, the timing and frequency of nocturia has no significant effect on SE, TST, and REM sleep duration; however, the presence of obstructive sleep apnea could negatively interfere with these parameters. Additionally, patients with nocturia episodes during superficial sleep did not have better SE or longer sleep times than patients experiencing deep sleep nocturia. Finally, the coexistence of obstructive sleep apnea and BPO could be an important factor contributing to the frequency of nocturia.

References


