Prevalence of Sleep Disordered Breathing among Patients with Nocturia at a Urology Clinic

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Abstract

Objective We assessed the prevalence of sleep disordered breathing (SDB) and characteristics among patients who visited a urology clinic complaining of nocturia (URO group) and those who visited a sleep apnea (SA) clinic complaining of excessive daytime sleepiness (EDS) (SA group). Additionally, we evaluated the effects of continuous positive airway pressure (CPAP) therapy in the URO group patients with nocturia and SDB resistant to conventional therapy for nocturia.

Methods Questionnaires were used to assess EDS, nocturia and lower urinary tract symptoms in 34 URO group patients and 49 age-matched SA group patients. We also compared these factors in the male patients in both groups and the male and female patients in the SA group. Significant SDB was diagnosed as a 3% oxygen desaturation index (3%ODI) on pulse oximeter of >5/h. The treatment response was analyzed in six URO group patients treated with CPAP after not responding to the conventional medical treatment.

Results SDB was found in 91.8% of the SA group patients and 70.6% of the URO group patients. The level of EDS and lower urinary tract symptoms were similar in both groups. The SA group showed higher 3%ODI values, while the frequency of urination during bedtime was higher in the URO group. The frequency of nocturnal urination was reduced after CPAP in the subjects resistant to conventional therapy.

Conclusion SDB is as prevalent in patients who visit a urology clinic complaining of nocturia as in those who visit a sleep apnea clinic. Patients who complain of nocturia must be assessed for SDB before starting therapy for nocturia.

Key words: nocturia, urology clinic, sleep apnea clinic, sleep disordered breathing, Continuous Positive Airway Pressure (CPAP)

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Introduction

Nocturia is known to not only be associated with worsening sleep quality and daytime quality of life, but it has also been shown to increase the incidence of hip fractures (1, 2), hypertension (3), coronary artery disease (4) and even mortality (5, 6). Recently, sleep disordered breathing (SDB) has been recognized as a cause of nocturia, along with benign prostatic hypertrophy (BPH) and overactive bladder (OAB) (7). As patients with nocturia usually visit urology clinics rather than sleep clinics, even if they feel sleepiness, SDB may be overlooked by many urologists, resulting in inadequate treatment for such patients. While many studies have examined the relationship between nocturia and SDB (8-11), no studies have investigated the prevalence or symptoms of SDB among patients visiting urology clinics who complain of nocturia (URO group) compared with patients visiting sleep clinics who complain of excessive daytime sleepiness, apnea or snoring (SA group).

Hence, the primary aim of this study was to assess the prevalence of SDB among URO patients and determine the differences in symptoms between the URO group and the SA group. The secondary aim was to assess whether continuous positive airway pressure (CPAP) therapy is effective for nocturia in patients with SDB who are resistant to con-
vntional medical therapy.

**Materials and Methods**

The participants were recruited from among the patients who visited a urology outpatient clinic complaining of nocturia (URO group, n=34) and age-matched patients who visited the sleep apnea clinic complaining of symptoms related to SDB, such as excessive daytime sleepiness (EDS), sleep apnea and snoring (SA group, n=49), at Saiseikai Futsukaichi Hospital.

The inclusion criteria for the participants were; 1) over 60 years of age for age matching and 2) no comorbidities with severe organic lower urinary tract disease. The exclusion criteria were as follows; 1) receiving treatment for SDB or nocturia at the time of the study and 2) severe organic lower urinary tract disease.

This study was approved by the ethics committee of Saiseikai Futsukaichi Hospital, and we collected data for consecutive patients analyzed retrospectively.

We examined EDS using the Japanese version of the Epworth sleepiness scale (JESS) questionnaire (12), assessed lower urinary tract symptoms (LUTS) using the international prostate symptom score (IPSS: seven questions about symptoms and one question about quality of life), evaluated the degree of SDB using a pulse oximeter (Pulsox, Teijin-Minolta, Tokyo, Japan) for one night at home and counted the frequency of nocturnal desaturation >≥3% in one hour [3% oxygen desaturation index (3%ODI)]. The frequency of nocturnal urination was obtained using a questionnaire.

Patients with a 3% ODI of >5 were defined as having SDB, as previously reported (13). The statistical analysis was performed using JMP 9 (SAS Institute, Cary, USA), and the data are presented as the mean ± standard deviation. Comparisons between groups were performed using the Wilcoxon test, with a p value of <0.05 considered to be statistically significant.

We compared age, gender, body mass index (BMI), 3% ODI, JESS, IPSS and nocturia between the URO group and the SA group. We also compared these parameters in males in the URO group (n=31) and the SA group (n=33) (††† in Table). There were no significant differences in the severity of daytime sleepiness or lower urinary tract symptoms between the two groups (JESS: 5.0±3.5 versus 5.5±4.1, p=0.72; IPSS: 12.4±5.8, 11.5±6.9, p=0.46, respectively). The mean age of the participants was older in the URO group (68.6±6.2 years versus 64.9±4.4 years, p=0.01). Additionally, the 3% ODI values were significantly higher in the SA group (9.6±8.5/h versus 38.4±18.9/h, p<0.0001), while the frequency of nocturnal urination was significantly higher in the URO group (3.1±1.1 versus 1.9±1.3, p<0.0001). In addition, we compared these parameters between males (n=33) and females (n=16) in the SA group (††† in Table). There were no significant differences in the severity of daytime sleepiness or lower urinary tract symptoms and nocturia between the two groups (JESS: 5.5±4.1 versus 6.6±4.6, p=0.42; IPSS: 11.5±6.9, 8.3±4.8, p=0.12, nocturia: 1.9±1.2 versus 2.0±1.3, p=0.91, respectively). Meanwhile, the mean age of the participants was higher in females (64.9±4.4 years versus 72.3±4.7 years, p<0.0001). Additionally, the 3% ODI values were significantly higher in males (38.4±18.9/h versus 18.3±18.0/h, p<0.0006) than in females in the URO group.

Although no significant correlations were observed between SDB and the frequency of nocturnal urination, more severe SDB was associated with severe nocturia (≥3 urinations per nights) in both groups (Fig. 1). No significant correlations were found between the severity of daytime sleepiness assessed according to the JESS score and the frequency of nocturnal urination.

In the URO group, conventional treatments for nocturia were offered to 17 patients with urological problems as well as SDB and seven patients with urological problems without SDB. Among these subjects, eight out of 17 patients with SDB (47.1%) and six out of seven patients without SDB (85.7%) showed an improvement in nocturia (Fig. 2). Among the six patients with SDB who were treated with CPAP, the mean frequency of nocturia was significantly re-
Discussion

While many studies have examined the relationship between nocturia and SDB (8-11), no previous studies have investigated the prevalence of SDB among patients specifically who visit urology clinics complaining of nocturia, specifically from the standpoint of a comparison with nocturia in those visiting sleep apnea clinics. Our study provides four important findings in this context. First, approximately 70% of the urology clinic patients complaining of nocturia had more than mild SDB. Second, there were no significant differences between the SA group and the URO group regarding symptoms of SDB and urological symptoms assessed using the JESS and IPSS scales. Third, the patients with more severe SDB tended to have more frequent nocturia. Lastly, patients complaining of nocturia who do not respond to conventional urological treatments are more likely to have SDB complications and might receive more benefit from therapy for SDB, such as CPAP.

Nocturia often develops after middle age (14). Nocturnal urination of ≥1 times per night occurs in as many as 69% of individuals in the general Japanese population and nocturnal urination of ≥3 times per night is reportedly observed in 14% of the general Japanese population ≥40 years of age (7). SDB, especially obstructive sleep apnea (OSA), has been recognized to be an important cause of nocturia. The
mechanisms underlying the development of nocturia in OSA patients are considered to be follows. Increased negative intrathoracic pressure generated by inspiration against the obstructed upper airway stretches the atrial and ventricular wall, resulting in the production of human atrial natriuretic peptide (ANP) from the atrium and brain natriuretic peptide (BNP) from the ventricle, both of which result in an increase in urine volume and consequent nocturia. Additionally, the occurrence of hypoxia during apnea or hypopnea itself has been reported to result in elevated BNP levels (15). Furthermore, one report showed that elevated ANP production during nighttime among SDB patients is likely due to both the outward stretch of the atrial muscles and hypoxia (16). Krieger demonstrated that CPAP therapy reduces the nocturnal ANP levels in patients without OSA (17). Therefore, changes in the natriuretic peptide level might be the main cause of increased urine volume in patients with SDB. In our study, approximately 70% of patients who visited the urology clinic complaining of nocturia had SDB and frequency of nocturia was higher in patients with SDB (9/18) than those without SDB (1/7).

Figure 2. Flow diagram of treatment and the results in patients who visited urology clinic complaining of nocturia. Among these patients, of 70.3 % (26/37) had SDB and frequency of patients who were resistant to urological conventional therapy was higher in patients with SDB (9/18) than those without SDB (1/7).

These results are understandable considering that the different subjective complaints of the patients led them to the different departments. In contrast, it is an interesting finding that there were no significant differences regarding the symptoms of SDB or urological symptoms assessed according to the JESS and IPSS scales between the two groups. We consider one possible reason for the lack of observed differences in the JESS and IPSS scores for the two groups is that: first, as they age, patients become less aware of EDS and LUTS (20), and, secondly, older persons have more urological diseases, such as BPH or OAB manifesting as LUTS (21, 22). It is also an interesting finding that there were significant differences in age between males in the URO and SA groups and in the prevalence of SDB between males and females in the SA group, although the reasons for this finding are not well explained.

The association between SDB and nocturia in the population under 50 years of age has been confirmed. However, no associations have been found between the frequency of nocturia and the symptoms of SDB in older populations, as in our patients (23). It was believed that an association between SDB and nocturia in the older population has not been confirmed due to the increased rate of urological symptoms leading to LUTS in elderly patients. It is also known that patients develop more symptoms of SDB as they age. In this study, although we did not find any significant relationships between SDB and the frequency of nocturia in the patients, the results indicated an increase in the frequency of nocturia as the SDB levels increased, as seen in Fig. 1. Further studies should clarify the relationship between SDB and nocturia in older population. However, as described above, it is important to note that, in this study, we found a high rate (70%) of SDB in the URO group (age >60), whereas the rate of SDB among the general population in Japan is reported to be 25% to 40% using the same definition of 3% ODI>5.

Although the sample size was small, the current study demonstrated a high success rate for CPAP treatment for nocturia with comorbidities of SDB when conventional urology treatment fails. At present, only a limited number of urologists may recognize SDB as being an important cause of nocturia and routinely look for this symptom in such patients. Our findings reinforce the importance of considering hidden SDB as a cause of nocturia, especially in those resistant to conventional urological therapy. Therefore, asking the patient whether they habitually snore or have apneic episodes when assessed at the outpatient clinic is the simplest and most important way to obtain the correct diagnosis and provide proper treatment for nocturia. Additionally, we wish to strongly recommend that urologists perform various simple but necessary tests, such as assessments with a pulse oximeter, to identify hidden SDB.

Our study is associated with some limitations. First, we used a pulse oximeter to assess SDB, rather than polysomnography (PSG). Compared to PSG, pulse oximetry is not a gold standard assessment tool; however, its benefits include...
easy application, cost effectiveness (24) and the ability to be used repeatedly. Since pulse oximeters have been used in many studies to diagnose SDB (13, 18, 19, 25, 26), we believe that we were able to diagnose SDB as accurately as that using PSG. Using a pulse oximeter was particularly essential in this study, as the study required the participation of patients from a urology outpatient clinic who did not have any self-awareness of their SDB symptoms. Therefore, pulse oximetry made it possible for many patients to participate in this study without the need for elaborate testing procedures. As our study was also quite small in size and retrospective, a larger scale prospective trial with polysomnography is necessary to attain more accurate information about this issue. Another limitation of the study includes the larger male sample size in the URO group compared to the SDB group at baseline. This may be attributed to the fact that males were more likely to have LUTS among the elderly population in this study (27), which is in contrast to the findings of previous reports showing no gender differences in the rate of perception of excessive daytime sleepiness in middle-aged patients with AHI>5/h (28). A case control study may be an alternative method to avoid this shortcoming.

In summary, this study indicated that approximately 70% of patients who visit urology clinics complaining of nocturia may also have SDB. Therefore, physicians in charge of taking care of patients with nocturia should routinely take the possibility of SDB into consideration in their practice, since therapy for SDB, such as CPAP, is fundamental for improving nocturia in these patients and may highly improve the patient’s quality of life.

Author’s disclosure of potential Conflicts of Interest (COI).
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References