Does frequency of nocturnal urination reflect the severity of sleep-disordered breathing?

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SUMMARY Nocturia is an often-described symptom of sleep-disordered breathing (SDB). The aim of our study was to determine the frequency of nocturnal urination among patients with different severity of SDB and to find out whether frequency of nocturnal urination reflects the severity of disease. A retrospective chart review was conducted among 1075 subjects of suspected SDB. Nocturia was assessed using standard questionnaire evaluating a frequency of nocturnal urination. Subjects were divided into four groups of SDB based on the polysomnographic evaluation. In primary snoring group, 51% subjects did not complain nocturia, 28% subjects reported one time, 16% subjects reported two to three times and 5% subjects reported more than three times urination per night. Among patients with mild obstructive sleep apnea syndrome (OSAS), nocturnal urination was not reported by 36% and was reported one time by 34%, two to three times by 15%, more than 3 times by 15%. The corresponding frequencies among patients with moderate OSAS were 40, 31, 17 and 12%, and with severe OSAS were 23, 22, 23 and 32%, respectively. The severe OSA group was significantly different from other groups as regards the frequency of nocturnal urination (P < 0.001) while other OSA groups did not show any significance. Nocturnal urination of more than three times was significantly more reported by severe OSA patients (P < 0.001) (positive predictive value = 0.71, negative predictive value = 0.62).

KEYWORDS nocturia, nocturnal urination, obstructive sleep apnea syndrome, polysomnographic evaluation, primary snoring, sleep-disordered breathing

Nocturia is an often-described symptom that may be associated with a variety of disorders including sleep-disordered breathing (SDB). The prevalence of nocturia was reported to be higher in male patients with obstructive sleep apnea syndrome (OSAS) than in age-controlled healthy male adults and there was also a significant improvement in the frequency of urination after appropriate therapy with nasal continuous positive airway pressure (Krieger et al. 1993; Warley and Stradling 1988).

The term nocturia has been used to refer to any awakening from sleep followed by urination although this may be overestimated (Barker and Mittness 1988; Resnick 1990). There are multiple and well-known pathological conditions, such as cardiovascular disease, hypertension (HT), diabetes mellitus (DM), lower urinary tract obstruction, behavioral and environmental factors resulting in nocturia. Although nocturia is common in SDB, the frequency of nocturnal urination in different severities of SDB has not been extensively studied before. The aim of our study was to determine the frequency of nocturnal urination among patients with different severities of SDB and to find out whether the number of nocturnal urinations reflects the severity of the disease. Such information may have implications for SDB case-finding and also assessment of SDB in the investigation of nocturia.

A retrospective chart review was conducted among patients who had been referred to our sleep laboratory for the evaluation of suspected SDB. The data were collected from the history, physical and polysomnographic evaluation.

Nocturia was assessed using a standard questionnaire evaluating an average frequency of urination per night.

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Responses were consolidated into four categories regarding the frequency of urination. These categories were: (1) not to awake with urination; (2) awake with urination one time per night; (3) awake with urination two to three times per night; and (4) awake with urination more than three times per night.

Polysomnographic (PSG) evaluation of a minimum of 8 h was performed on Embla A10 (Flaga, Reyjavick, Iceland) and Somnostar Alpha (Sensormedics, Yorba Linda CA, USA) sleep systems.

Inclusion criteria included age > 19 years, symptoms consistent with SDB, satisfactory control of cardiovascular disease (CVD), HT, and DM. Patients with known prostate enlargement, as diagnosed by private physicians or ourselves, alcoholism, drug abuse, taking diuretic drugs, having uncontrolled CVD, HT, DM and demonstrated central sleep apnea or other sleep disorders were excluded from the study.

Demographic variables were defined as age, gender and body mass index (BMI). HT, CVD and DM were determined as clinical variables and RDI and lowest oxygen saturation point during abnormal respiratory events were determined as PSG variables.

Data from 1075 patients were analyzed. SDB was determined by using four RDI cut-off points (RDI ≤ 5, 5 < RDI ≤ 15, 15 < RDI ≤ 30 and RDI > 30) and patients were divided into four groups based on the PSG evaluation.

For a group as a whole, partial correlation analysis was performed to detect the relationships between frequency of nocturnal urination and PSG. As the frequency of urination is influenced by age and gender, partial correlations were also run with controlling for age in a whole group and in male and female patients separately.

Four groups of SDB patients were compared with chi-square test and one-way analysis of variance (ANOVA) with Tukey HSD post-hoc comparisons regarding frequency of nocturnal urination and PSG. As the frequency of urination is influenced by age and gender, partial correlations were also run with controlling for age in a whole group and in male and female patients separately.

The group included 246 women and 829 men with a mean age of 49 ± 11 years (range: 20–80 years). The mean RDI was 33 ± 29 (range 0–144) and mean lowest oxygen saturation was 81 ± 11% (range 40–98%).

The demographic, polysomnographic and clinical characteristics of four groups of SDB patients are represented in Table 1. Subjects with primary snoring were significantly younger than OSA patients while there was no significant difference between OSA patients with respect to age (F = 18, 46, P < 0.001). On the contrary, severe OSA patients had significantly higher BMI than other groups of SDB patients while moderate OSA patients had significantly higher BMI than subjects with primary snoring (F = 50, 61, P < 0.001). In respect of lowest oxygen saturation, primary snoring subjects had significantly higher and severe OSA patients had significantly lower mean lowest oxygen saturation than other groups of patients. However, mild and moderate OSA patients were not different with respect to lowest oxygen saturation point.

The prevalence of DM and HT was significantly different between SDB groups (P < 0.005, P < 0.001) while no significant difference was obtained for CVD.

For a group as a whole, significant correlations were determined between the frequency of nocturnal urination and mean age (r = 0.29, P < 0.001), BMI (r = 0.29, P < 0.001), RDI (r = 0.34, P < 0.001) and lowest oxygen saturation (r = −0.36, P < 0.001). Controlling for age for all patients, frequency of nocturnal urination also showed significant correlations with mean BMI (r = 0.29, P < 0.001), RDI (r = 0.32, P < 0.001), and lowest oxygen saturation (r = −0.34, P < 0.001). Furthermore, significant correlations were also obtained in both male (r = 0.26, P < 0.001), (r = 0.28, P < 0.001), (r = 0.36, P < 0.001), (r = −0.37, P < 0.001), and female (r = 0.35, P < 0.001), (r = 0.32, P < 0.001), (r = 0.33, P < 0.001), (r = −0.39, P < 0.001) patients.

Polysomnographic evaluation revealed that 21% subjects had primary snoring, 19% patients had mild OSAS, 16% patients had moderate OSAS and 44% patients had severe OSAS.

The frequency of nocturnal urination in four groups of SDB patients is shown in Fig. 1. In the primary snoring group, 51% subjects did not complain of nocturia at all while 28% subjects reported once, 16% subjects reported two to three times and 5% subjects reported more than three times urination per night. Among patients with mild OSAS, nocturnal urination was not reported by 36% and was reported once per night by 34%, two to three times per night by 15%, more than three times per night by 15%. The corresponding frequencies among

Table 1 Demographic, polysomnographic and clinical characteristics of sleep-disordered breathing patients

<table>
<thead>
<tr>
<th></th>
<th>Primary snoring (RDI ≤ 5; n = 229)</th>
<th>Mild OSAS (5 &lt; RDI ≤ 15; n = 199)</th>
<th>Moderate OSAS (15 &lt; RDI ≤ 30; n = 169)</th>
<th>Severe OSAS (RDI &gt; 30; n = 478)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
<td>44 ± 10</td>
<td>49 ± 10</td>
<td>51 ± 11</td>
<td>50 ± 11</td>
<td>0.0000</td>
</tr>
<tr>
<td>% Male</td>
<td>60</td>
<td>76</td>
<td>80</td>
<td>85</td>
<td>0.0000</td>
</tr>
<tr>
<td>BMI (kg m⁻²)</td>
<td>27 ± 4</td>
<td>29 ± 4</td>
<td>29 ± 5</td>
<td>32 ± 6</td>
<td>0.0000</td>
</tr>
<tr>
<td>L. Oxygen (%)</td>
<td>92 ± 3</td>
<td>86 ± 5</td>
<td>83 ± 5</td>
<td>72 ± 11</td>
<td>0.0000</td>
</tr>
<tr>
<td>HT (%)</td>
<td>31 (13.5)</td>
<td>47 (23.6)</td>
<td>36 (21.3)</td>
<td>144 (30.1)</td>
<td>0.00022</td>
</tr>
<tr>
<td>CVD (%)</td>
<td>9 (3.9)</td>
<td>12 (6)</td>
<td>15 (8.8)</td>
<td>37 (7.7)</td>
<td>0.17</td>
</tr>
<tr>
<td>DM (%)</td>
<td>5 (2.1)</td>
<td>6 (3)</td>
<td>12 (7.1)</td>
<td>43 (8.9)</td>
<td>0.0008</td>
</tr>
</tbody>
</table>

OSAS, obstructive sleep apnea syndrome; BMI, body mass index; L. oxygen, lowest oxygen saturation during apneas and hypopneas; HT, hypertension; CVD, cardiovascular disease; DM, diabetes mellitus. Continuous variables are expressed as mean ± SD.
The frequency of nocturnal urination showed significant differences between the four groups of SDB ($P < 0.001$). The comparison of SDB groups revealed that severe OSA group was significantly different from other groups regarding the frequency of nocturnal urination categories ($P < 0.001$). Nocturnal urination of more than three times per night was reported more significantly by severe OSA patients than other groups of SDB patients ($P < 0.001$) (positive predictive value $= 0.71$, negative predictive value $= 0.62$). Performing chi-square test by excluding severe OSA group showed that mild and moderate OSA groups did not show significance with respect to frequency of nocturnal urination while any nocturia complaint was significantly more reported in primary snoring group than mild–moderate OSA groups ($P < 0.01$).

Our results shows that nocturnal urination increases with increasing SDB severity and more than three urinations per night is mostly associated with severe OSAS.

This association may not be independent of coexistence of other factors as our subjects were not matched for age and co-morbid factors that may promote nocturia. It was not the aim of this study to determine whether SDB causes pathological nocturia. For this purpose a larger number of controls matched for age, gender and other co-morbidities would be needed. Moreover, factors promoting or related to pathological nocturia are also frequently associated with SDB. Previous studies showed that the prevalence of nocturia increase with advancing age and appears to be common in women as in men (Asplund and Aberg 1992; Malmsten et al. 1997; Swithinbank et al. 1997). Age is a well-known risk factor for OSAS and does not deserve further comment. However, patients with severe OSA had a mean age of 50 years in our study, which is probably too young for the occurrence of high prevalence of nocturia more than three times. In addition, although there was no significant difference between the OSA groups with respect to age, the severe OSA group was significantly different from the other groups with a higher prevalence of nocturnal urination more than three times. Male gender is also another risk factor for OSAS and the reported male : female ratio for the prevalence of SDB was ca. 3 : 1 (Young et al. 1993). The prevalence of pathological nocturia is greater among females than males with OSAS (Hajduk et al. 2003). The relatively small size of females in our study population does not allow us to speculate that pathological nocturia is more common in males than in females with OSAS. The diseases leading to nocturia include CVD, DM and lower urinary tract obstruction (Asplund and Aberg 1992; Barker and Mittness 1988; Klein et al. 1999). These pathological conditions causing nocturia are also highly associated with SDB. The prevalence of HT increased significantly with the increase in the severity of SDB. (Nieto et al. 2000). OSAS was found in 65% of subjects with DM and those with moderate–severe OSAS had significantly greater overnight urine production than subjects without OSAS. (Chasens et al. 2002). The prevalence of HT and DM showed significant differences between SDB groups in our study with a higher prevalence in severe OSAS patients than in the other groups. Because of the high association of co-morbidities of nocturia and risks and associated factors of SDB, we cannot completely rule out the possibility that the increased prevalence of pathological nocturia can be explained, at least in part, by other factors associated with SDB. However, it must be emphasized that only the patients with controlled HT and DM were included the study.

We conclude that nocturnal urination more than three times is common in severe OSAS and important for the clinical prediction of disease severity. In the evaluation of SDB, the
clinician should have a high degree of suspicion for severe OSAS in subjects with nocturia complaint of more than three times.

REFERENCES


