TÜBİTAK

Turkish Journal of Medical Sciences

http://journals.tubitak.gov.tr/medical/

Research Article

Turk J Med Sci
(2014) 44: 249-254
© TÜBİTAK
doi:10.3906/sag-1210-20

The association of nocturia with sleep disorders and metabolic and chronic pulmonary conditions: data derived from the polysomnographic evaluations of 730 patients

Sibel AYIK[1,*], Kaan BAL[2], Galip AKHAN[3]

[1]Department of Pulmonary Diseases, Faculty of Medicine, İzmir Katip Çelebi University, İzmir, Turkey
[2]Department of Urology, Faculty of Medicine, İzmir Katip Çelebi University, İzmir, Turkey
[3]Department of Neurology, Faculty of Medicine, İzmir Katip Çelebi University, İzmir, Turkey

Received: 05.10.2012 • **Accepted:** 26.02.2013 • **Published Online:** 15.01.2014 • **Printed:** 14.02.2014

Aim: To evaluate the prevalence of nocturia among different degrees of obstructive sleep apnea (OSA) and its association with various clinical conditions.

Materials and methods: In 730 OSA patients, the prevalence and frequency of nocturia was determined, and the association of nocturia with clinical and laboratory variables such as the apnea–hypopnea index (AHI), apnea duration, and minimum oxygen saturation and clinical conditions such as diabetes mellitus, coronary heart disease, and chronic obstructive pulmonary disease (COPD) was determined.

Results: The overall prevalence of nocturia (≥2 wakes/night) was 50.9%. Prevalences of nocturia in simple snoring and mild, moderate, and severe OSA patients were 40.6%, 44.4%, 58.6%, and 57.1%, respectively ($P < 0.005$). The frequency of nocturia significantly increases with the severity of OSA (1.4 ± 1.0 wakes/night in mild OSA vs. 2.0 ± 1.4 wakes/night in severe OSA, $P = 0.001$). Age, AHI, average oxygen saturation, and presence of diabetes mellitus, hypertension, and COPD were found to be significant risk factors associated with nocturia ($P < 0.001$).

Conclusion: The frequency of nocturia increases as the severity of OSA increase. The increased prevalence of nocturia in patients with OSA, diabetes mellitus, hypertension, and COPD indicates the complex physiological background of this bothersome urologic symptom.

Key words: Sleep, apnea, nocturia

1. Introduction

Obstructive sleep apnea (OSA) is a disorder characterized by repetitive, complete, or partial obstruction of the upper airways, and it is usually associated with a reduction in blood oxygen saturation. Major symptoms, namely snoring, witnessed apnea, and excessive daytime sleepiness, are sometimes accompanied by minor symptoms such as sweating, dry mouth, headache, and intellectual disorders (1).

Nocturia, which is defined as waking to pass urine after falling asleep at night, is not uncommon in patients with OSA. In 2002, the International Continence Society defined nocturia as waking at night to void. This definition covers any number of voids in which patients wake up from sleep (2). It is one of the most common reasons for sleep interruption in the adult population of both sexes. The incidence of nocturia increases with age (3,4). The etiology of nocturia is complex, but the symptom results from any of the following conditions: diurnal polyuria, nocturnal polyuria, and low bladder capacity. Nocturia is also found to be associated with aging, overactive bladder, benign prostatic obstruction in men, medications (diuretics, analgesics), or chronic clinical conditions such as diabetes mellitus, diabetes insipidus, anorexia nervosa, congestive heart failure causing peripheral edema, and sleep disturbances (5).

The prevalence of nocturia in OSA patients ranges between 48% and 76% depending on the number of night time voids accepted to be pathologic (6–8). It has been shown that the frequency of nocturia in patients with OSA is significantly higher than in healthy controls (9,10). Moreover, it has been shown that as the severity of OSA increases, the frequency of nocturia increases, as well (6,8). Interestingly, the frequency of nocturia tends to decrease when OSA is treated with continuous positive airway pressure (11,12).

* Correspondence: sibeloktem2000@gmail.com

It seems that there is an association between upper airway obstruction and nocturia. In this large retrospective series we searched for the fundamentals of this association. In our work we evaluated the prevalence of nocturia among patients suffering from different degrees of OSA and the association of nocturia with laboratory parameters recorded during polysomnography (PSG). We also evaluated the association of nocturia with chronic clinical conditions such as diabetes mellitus, hypertension, chronic obstructive pulmonary disease (COPD), and coronary heart disease.

2. Materials and methods

We retrospectively evaluated the polysomnographic recordings of 730 patients (256 females, 474 males) who were referred to our sleep center with the suspected diagnosis of OSA. The age of the patients ranged between 19 and 80 years. All patients completed a patient evaluation questionnaire before PSG, which was carried out with the Alice 5 Diagnostic Sleep System set (version 2007, Philips Respironics) in the sleep laboratory, and a single overnight PSG result was obtained for each patient.

2.1. Patient exclusion criteria and Epworth Sleepiness Scale

Patients with known benign prostate hyperplasia; patients with uncontrollable or poorly controlled congestive heart failure, diabetes mellitus, chronic renal failure, COPD, or hypertension; patients with drug or alcohol addiction; and patients diagnosed to have other types of sleep disorders such as restless leg syndrome, periodic leg movements in sleep, REM disturbances, and central sleep apnea were excluded from the study.

Daytime sleepiness of the patients was evaluated by Epworth Sleepiness Scale (ESS). The ESS is a brief questionnaire that subjectively measures an individual's likelihood of falling asleep in real life situations such as sitting, reading, watching TV, or driving. Scores range from 0 to 24, where higher scores correlate with increased sleepiness. When used as a screening tool, scores over 8 indicate the need for a consultation from a sleep specialist.

2.2. Evaluation of nocturia

Nocturia was evaluated by 2 questions: "During the past 5 days, did you wake up to void at night after you fell asleep?" and "During the past 5 days, how many times did you wake up to urinate at night after you fell asleep?"

2.3. Polysomnography

PSG was carried out with the Alice 5 Diagnostic Sleep System set (version 2007, Phillips Respironics). During PSG, recordings of central and occipital electroencephalography, submental electromyography (EMG), bilateral electrooculogram, airflow, patient position, bilateral anterior tibial EMG, electrocardiogram, respiratory efforts, pulse oximeter, and video monitorization of the patients were obtained. Patients entered the test room at 2000 hours. The lights were turned off at 2200 hours and recordings began. Polysomnograms were performed and reported by a certified specialist who was one of the coauthors of this article (SA). Sleep stages were classified according to the criteria of Rechtschaffen and Kales (13). Respiratory parameters of the patients were classified according to criteria set by the American Academy of Sleep Medicine. Complete secession of oronasal air flow for longer than 10 s was defined as an apnea. A decrease in oxygen saturation by 3% for a period of longer than 10 s or arousal with a 50% decrease in oronasal airflow was defined as hypopnea. The number of apneas and hypopneas recorded in 1 h was defined as the apnea–hypopnea index (AHI) (14).

The severity of OSA was graded as follows:

Patients with an AHI score of <5 were labeled as having simple snoring (normal), patients with an AHI score between 5 and 15 were diagnosed with mild OSA, patients with an AHI value between 15 and 30 were diagnosed with moderate OSA, and patients with an AHI value of ≥30 were diagnosed with severe OSA (15).

The following variables were evaluated for their association with the frequency of nocturia:

- Demographic variables such as age, sex, body mass index, neck circumference, and comorbid conditions such as diabetes mellitus, hypertension, coronary heart disease, and chronic pulmonary lung disease;
- Score on the ESS;
- Polysomnographic parameters such as AHI, minimum saturation, mean saturation, and longest apnea duration.

2.4. Statistical analysis

The mean, median, and standard deviation were used in the descriptive analysis of the variables. Analysis of variance was used in the multiple group comparisons of continuous variables. The Tukey test was used in the post hoc analysis. The chi-square test was used to compare frequencies of variables between groups. Multiple logistic regression analysis within a confidence interval of 95% was performed to estimate the relative risk of factors affecting nocturia frequency. P-values of less than 0.05 were accepted as having statistical significance. All calculations were performed by SPSS 11.0.

3. Results

There were 160 (22%) patients who had simple snoring. There were 160 (22%) patients with mild OSA, 128 (17.5%) with moderate OSA, and 282 (38.5%) with severe OSA. The percentage of patients having nocturia ≥2 times per night was similar in male and female patient groups

(51.3% vs. 50.4%). Patients with simple snoring were found to be younger, and female patients predominated in this group. These patients had smaller body mass indexes and narrower neck circumferences. Patients in the mild, moderate, and severe OSA groups were older and had more comorbidities when compared to patients in the simple snoring group. Patients with severe OSA were mostly male, were older, and had greater neck circumferences and body mass indexes and increased Epworth scale values. Table 1 shows the demographic characteristics (age, sex, body mass index, and neck circumference) and comorbid conditions of patients grouped according to OSA severity.

Seventy-five patients (10.3%) did not report any nocturia in their patient evaluation form. The percentage of patients who reported 1, 2, 3, and ≥4 nocturia episodes per night were 38.8%, 27.3%, 13.8%, and 9.9%, respectively (Table 2). The frequency of nocturia significantly increased as the severity of OSA increased (1.4 ± 1.0 wakes/night in mild OSA vs. 2.0 ± 1.4 wakes/night in severe OSA, P = 0.001). A statistically significant majority of patients with ≥4 nocturia episodes were in the severe OSA group (39 of 72 patients, 54.2%; Pearson chi-square, P < 0.001). Most of the patients who did not report any nocturia were in the simple snoring and mild OSA groups (45 of 75 patients, 60%). The percentage of patients having any frequency of nocturia was highest in the moderate and severe OSA groups, followed by the mild OSA and simple snoring groups (93.8% and 92.2% vs. 85% and 87%, respectively; Pearson chi-square, P < 0.005; Table 2). When patients were further grouped as having nocturia frequency of less than and more than 2 episodes per night, the percentage of patients with 2 or more nocturia episodes was 50.9%. (40.6% in the simple snoring group, 44.4% in the mild OSA group, 58.6% in the moderate OSA group, and 57.1% in the severe OSA group) (Pearson chi-square, P < 0.001; Table 2).

The frequency of OSA and nocturia both increased significantly as age increased. Figures 1 and 2 show the age group distribution of OSA severity and nocturia frequency.

The percentages of hypertension (65.5%), diabetes mellitus (70.3%), coronary artery disease (68.3%), and COPD (77.8%) were significantly higher among patients with nocturia ≥2 times per night.

In a multivariate logistic regression analysis we found that age, AHI, average oxygen saturation, and presence of diabetes mellitus, hypertension, and COPD had a significant effect on the frequency of nocturia. Relative risk ratios and confidence intervals of these variables are shown in Table 3.

4. Discussion

Nocturia is one of the most bothersome urinary tract symptoms, and it has a negative impact on both sleep quality and health-related quality of life. This urinary tract symptom is frequently seen in OSA patients. Depending on the number of night-time voids accepted to be pathological, the prevalence of nocturia in OSA ranges between 48% and 76% (6–8). Supporting the previously

Table 1. Clinical and demographical characteristics, nocturia frequency, and comorbid conditions of patients grouped according to OSA severity.

	A (n = 160), simple snoring	B (n = 160), mild OSA	C (n = 128), moderate OSA	D (n = 282), severe OSA	P
Age, years	42.8 ± 11.6	50.0 ± 10.9	53.0 ± 15.2	50.5 ± 10.2	<0.005 a
Body mass index, kg/m^2	28.9 ± 5.2	30.6 ± 4.9	31.0 ± 5.0	33.3 ± 6.1	<0.005 b
ESS	6.38 ± 4.6	7.31 ± 4.8	7.32 ± 4.8	9.7 ± 5.5	<0.005 c
Neck circumference, cm	37.0 ± 3.2	39.6 ± 3.6	40.2 ± 2.9	41.9 ± 3.4	<0.005 d
Nocturia frequency, per night	1.4 ± 1.0	1.6 ± 1.3	1.9 ± 1.2	2.0 ± 1.4	<0.005 e
Sex: female, % (n)	59.4 (95)	36.7 (59)	32.8 (42)	21.3 (60)	0.005 f
COPD, %	2.0	4.1	9.7	5.5	0.03 g
HT, %	7.2	21.6	27.4	25.8	0.001 h
DM, %	3.9	10.1	16.1	12.0	0.008 i
CAD, %	3.3	4.1	7.3	7.6	0.2

COPD: chronic obstructive pulmonary disease; HT: hypertension; DM: diabetes mellitus; CAD: coronary artery disease.
a: A < B, C, D; b: A < B = C < D; c: A = B = C < D; d: A < B = C < D, e: A < B < C < D; f: D < B = C < A; g. A = B = D < C; h: A < B = C = D; i: A < B = C = D.

Table 2. Distribution of nocturia frequency of patients among OSA groups.

Nocturia frequency	A (n = 160), simple snoring	B (n = 160), mild OSA	C (n = 128), moderate OSA	D (n = 282), severe OSA	n = 730, total
None, n (%)	21 (28)	24 (32)	8 (10.7)	22 (29.3)	75 (10.3%)
1 per night, n (%)	74 (26.1)	65 (23)	45 (16)	99 (34.9)	283 (38.8%)
2 per night, n (%)	43 (21.6)	37 (18.6)	48 (24.1)	71 (35.7)	199 (27.2%)
3 per night, n (%)	15 (14.9)	20 (19.7)	15 (14.9)	51 (50.5)	101 (13.8%)
≥4 per night, n (%)	7 (9.7)	14 (19.4)	12 (16.7)	39 (54.2)	72 (9.9%)
Any frequency of nocturia	139 (87%)	136 (85%)	120 (93.8%)	260 (92.2%)	655 (90%)
Nocturia ≥2 times per night	65 (40.6%)	71 (44.4%)	75 (58.6%)	161 (57.1%)	372 (60%)

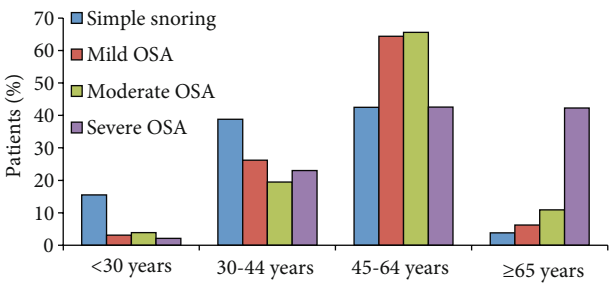

Figure 1. The distribution of OSA severity among age groups.

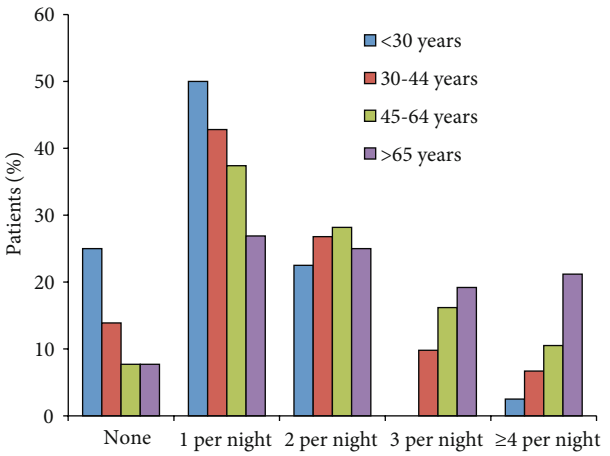

Figure 2. The distribution of nocturia frequency among age groups.

Table 3. Relative risk ratios and confidence intervals of age, AHI, diabetes mellitus, hypertension, COPD, and average oxygen saturation.

Variable	Beta	Odds ratio	95% CI for exp(B)	Significance
Age	0.028	1.028	1.013–1.044	0.000
AHI	0.012	1.012	1.005–1.019	0.000
Average oxygen saturation	0.083	0.921	0.892–0.950	0.000
COPD	1.115	0.328	0.146–0.739	0.007
HT	0.534	0.586	0.389–0.883	0.011
DM	0.081	0.999	0.001–0.130	0.044

reported data, in this study we also found an increased frequency of nocturia as the severity of OSA increased. We found that the percentage of nocturic patients was higher in the moderate and severe OSA groups than in the mild OSA and simple snoring groups (94% and 92% vs. 85% and 87%, respectively; Pearson chi-square, $P < 0.005$). The percentage of patients having ≥2 nocturia episodes was 50.9% (40.6% in simple snoring group and 44.4% in the mild, 58.6% in the moderate, and 57.1% in the severe OSA groups) (Pearson chi-square, $P < 0.001$).

When compared with the literature, these percentages are very high, and higher nocturia rates in the moderate OSA group contradict previously reported data from other authors. A possible explanation for this may derive from the patient characteristics and study design. It is well known that the incidence of nocturia increases with age and it may result from diurnal polyuria, nocturnal polyuria, or low bladder capacity (5). Since our study was retrospective in design, the accumulation of elderly patients in the moderate OSA group or the predominance of male patients who could have had nocturia as a result of benign prostate hyperplasia may have contributed to this increased percentage. Moreover, in the moderate OSA group, there were more patients with coronary heart disease, COPD, and hypertension, which might also have affected the frequency of nocturia.

Although there are controversial results with regard to male or female predominance in nocturia (6,10,16), in our study, we found no difference in the prevalence of nocturia between the sexes.

Several factors have been identified that effect the frequency of nocturia in OSA patients. Besides demographic factors such as age, sex, body mass index, and comorbid situations, laboratory parameters such as AHI, arousal index, and changes in blood oxygen saturation were found to be related with frequency of nocturia in OSA (6,8,10,16–18).

The effect of age on the frequency of nocturia is well known. The prevalence of nocturia in the population increases from 10% in a young population up to 64%–80% in the elderly (16,19–20). Likewise, aging is also related to OSA, whereby the diagnosis of OSA peaks between the fourth and sixth decades (6,20). Similarly, the majority of our patients (60.8%) were between 45 and 64 years of age, and 42.6% of them were diagnosed to have severe OSA. Moreover, the percentage of patients who had a nocturia frequency of ≥4 was significantly higher in patients between 45 and 64 years of age. In our study, logistic regression analysis showed that aging increases nocturia frequency by 2.1%.

Obesity is a known risk factor for OSA and the prevalence of nocturia increases among obese and morbidly obese patients. In the literature there are studies reporting an association between obesity and increased frequency of nocturia in patients with OSA (12,13,16,18). In our study, although patients with moderate and severe OSA had increased body mass index and neck circumferences, we failed to demonstrate any effect of these parameters on the frequency of nocturia. This may be due to the fact that our patient population was a rather homogeneous group with regard to body mass index and neck circumference. Therefore, when there are no extreme values (i.e. morbidly obese patients), the effect will probably be subtle.

When we examined the PSG parameters we found that AHI and average oxygen saturation, which are the indicators of apnea and hypoxia, were independent variables affecting nocturia frequency. Several mechanisms take part in the occurrence of nocturia in patients with OSA (10,18). Repetitive episodes of hypoxia during apnea and alterations in intrapleural negative pressure will affect the right atrium, resulting in increased atrial natriuretic peptide (ANP) secretion. Increased levels of ANP will result in inhibition of the renin–angiotensin–aldosterone system, eventually causing increased sodium and urine excretion (21–23). Furthermore, increased sympathetic activity in OSA patients causes increased urine production and hyperactivity of bladder smooth musculature (10).

OSA may coexist with COPD, diabetes mellitus, hypertension, coronary artery disease, and monosymptomatic enuresis nocturia in children (18,24). Moreover it has been reported that OSA is associated with lower urinary tract symptoms and a significant improvement of symptoms can be achieved when OSA is treated (25). The coexistence of COPD and OSA is very common, due to the same risk factors underlying these 2 clinical entities. Nocturia is frequently seen in COPD cases due to hypoxia, frequent awakenings, and anticholinergic medication. In our study we found that OSA patients having these conditions had increased nocturia prevalence; however, in logistic regression analysis only hypertension, diabetes mellitus, and COPD were found to be risk factors affecting the frequency of nocturia.

In conclusion, nocturia is closely associated with OSA. The frequency of nocturia per night increases as the severity of OSA increases. The increased prevalence of nocturia in OSA, diabetes mellitus, hypertension, and COPD indicates the complex physiological background of this bothersome urologic symptom. Therefore, when evaluating a patient for nocturia, these associated factors should be kept in mind. A better understanding of nocturia and its association with different clinical conditions would help clinicians to tailor an individualized approach according to the patient's condition.

References

1. Collop NA, Cassel DK. Snoring and sleep disordered breathing. In: Chiong TLL, Sateie MJ, Carskadon MA, editors. Sleep Medicine. Philadelphia, PA, USA: Hanley and Belfus; 2002. pp. 349–55.
2. van Kerrebroeck P, Abrams P, Chaikin D, Donovan J, Fonda D, Jackson S, Jennum P, Johnson T, Lose GR, Mattiasson A et al. The standardization of terminology in nocturia: report from the Standardization Sub-committee of the International Continence Society. BJU 2002; 90 (Suppl. 3): 11–5.
3. Abrams P. Nocturia: the effect on sleep and health consequences. Eur Urol Supplements 2005; 3: 1–7.
4. Schatzl G, Temml C, Schmidbauer J, Dolezal B, Haidinger G, Madersbacher S. Cross-sectional study of nocturia in both sexes: analysis of a voluntary health screening project. Urology 2000; 56: 71–5.
5. Abrams P. Nocturia: the major problem in patients with lower urinary tract symptoms suggestive of benign prostatic obstruction (LUTS/BPO). Eur Urol Supplements 2005; 3: 8–16.
6. Hajduk IA, Strollo PJ, Jasani RR, Atwood CW, Houck PR, Sanders MH. Prevalence and predictors of nocturia in obstructive sleep apnea-hypopnea syndrome – a retrospective study. Sleep 2003; 26: 61–4.
7. Kaynak H, Kaynak D, Oztura I. Does frequency of nocturnal urination reflect the severity of sleep-disordered breathing? J Sleep Res 2004; 13: 173–6.
8. Oztura I, Kaynak D, H C Kaynak. Nocturia in sleep-disordered breathing. Sleep Med 2006; 7: 362–7.
9. Krieger J, Petiau C, Sforza E, Delanoe C, Hecht MT, Chamouard V. Nocturnal pollakiuria is a symptom of obstructive sleep apnea. Urol Int 1993; 50: 93–7.
10. Umlauf MG, Chasens ER. Sleep disordered breathing and nocturnal polyuria: nocturia and enuresis. Sleep Med Rev 2003; 7: 403–11.
11. Margel D, Shochat T, Getzler O, Livne PM, Pillar G. Continuous positive airway pressure reduces nocturia in patients with obstructive sleep apnea. Urology 2006; 67: 974–7.
12. Krieger J, Follenius M, Sforza E, Brandenberger G, Peter JD. Effects of treatment with nasal continuous positive airway pressure on atrial natriuretic peptide and arginine vasopressin release during sleep in patients with obstructive sleep apnoea. Clin Sci 1991; 80: 443–9.
13. Rechtschaffen A, Kales A. A Manual of Standardized Terminology, Techniques, and Scoring System for Sleep Stages of Human Subjects. Los Angeles, CA, USA: UCLA Brain Research Institute; 1968.
14. Iber C, Ancoli-Israel S, Chesson AL Jr, Quan SF. The AASM Manual for the Scoring of Sleep and Associated Events: Rules, Terminology and Technical Specifications. 1st ed. Westchester, IL, USA: American Academy of Sleep Medicine; 2007.
15. American Academy of Sleep Medicine. International Classification of Sleep Disorders (ICSD): Diagnostic and Coding Manual. 2nd ed. Westchester, IL: American Academy of Sleep Medicine; 2005.
16. Yoshimura K, Terada N, Matsui Y, Terai A, Kinukawa N, Arai Y. Prevalence of and risk factors for nocturia: analysis of a health screening program. Int J Urol 2004; 11: 282–7.
17. Klein BE, Klein R, Lee KE, Bruskewitz RC. Correlates of urinary symptom scores in men. Am J Public Health 1999; 89: 1745–8.
18. Parthasarathy S, Fitzgerald MP, Goodwin JL, Unruh M, Guerra S, Quan SF. Nocturia, sleep-disordered breathing, and cardiovascular morbidity in a community-based cohort. PLoS ONE 2012; 7: e30969.
19. Garraway WM, Collins GN, Lee RJ. High prevalence of benign prostatic hypertrophy in the community. Lancet 1991; 24: 469 –71.
20. Hale WE, Perkins LL, May FE, Marks RG, Stewart RB. Symptom prevalence in the elderly. An evaluation of age, sex, disease, and medication use. J Am Geriatr Soc 1986; 34: 333–40.
21. Lin CC, Tsan KW, Lin CY. Plasma levels of atrial natriuretic factor in moderate to severe obstructive sleep apnea syndrome. Sleep 1993; 16: 37–9.
22. Follenius M, Krieger J, Krauth MO, Sforza F, Brandenberger G. Obstructive sleep apnea treatment: peripheral and central effects on plasma renin activity and aldosterone. Sleep 1991; 14: 211–7.
23. Arai H, Furuta H, Kosaka K. Polysomnographic and urodynamic changes in a case of obstructive sleep apnea syndrome with enuresis. Psychiatry Clin Neurosci 1999; 53: 319–20.
24. Gökçe A, Aslan S, Yalçınkaya FR, Davarcı M, Kaya YS, Savaş N, Görür S, Dağlı Ş, Kiper AN, Balbay MD. Improvement of monosymptomatic enuresis after adenotonsillectomy in children with obstructive sleep apnea syndrome. Turk J Med Sci 2012; 42: 757–61.
25. Odabaş Ö, Ceylan C, Yığman M. Does the treatment of obstructive sleep apnea syndrome improve lower urinary tract symptoms? Turk J Med Sci 2012; 42: 619–22.