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The effect of continuous positive airway pressure on nocturia in patients with obstructive sleep apnea syndrome

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Abstract

Objective: The prevalence of nocturia in patients with obstructive sleep apnea syndrome (OSAS) who received continuous positive airways pressure (CPAP) treatment was studied as well as the effect of CPAP treatment on nocturia.

Methods: All patients that were referred to the pulmonology department of a large teaching hospital in the Netherlands and received a CPAP mask for OSAS were interviewed and invited to take part in the study (N = 274). After informed consent, all patients were asked about the number of nocturia episodes before and after CPAP.

Results: In this prospective analysis, 274 patients (190 male and 84 female) were included. The mean age was 60.3 years (SE = 0.7). Sixty-four patients (23.4%) reported no nocturia episodes before CPAP and 210 patients (76.4%) reported ≥ 1 nocturia episode(s). Treatment of OSAS with CPAP reduced nocturia with one or more episodes per night in 42.3% of the patients. Clinically relevant nocturia (≥ 2 voids per night) was reduced from 73.0% to 51.5%. There were no statistically significant gender differences.

Conclusion: The prevalence of nocturia in patients diagnosed with OSAS is 75.8% in both sexes. After treatment with CPAP, almost half of patients experienced a decrease in the nocturia frequency of one or more voids. Clinically relevant nocturia was reduced with one-third after CPAP. CPAP not only reduced the number of voids during the night but also improved the associated quality of life.

KEYWORDS

CPAP, nocturia, OSAS

1 | INTRODUCTION

Obstructive sleep apnea syndrome (OSAS) is a chronic sleep disorder characterized by recurrent episodes of obstruction of the upper airway causing intermittent hypoxemia and hypercapnia and sleep fragmentation.¹ These adverse effects of

OSAS are important mediators of metabolic, cardiovascular, and neurocognitive risk.² Because of the nonspecific symptoms, OSAS often remains undiagnosed.

Several studies suggest that nocturia may be related to OSAS.^{3–5} Oztura et al⁶ found that OSAS was significantly associated with nocturnal urination in 1970 patients with

OSAS. In patients with OSAS, nighttime frequency of more than once is reported to be 52% to 77%, depending on the severity of sleep-disordered breathing.^{6,7}

The mechanisms by which OSAS induces nocturia have not been elucidated and a few mechanisms have been suggested to be involved in the pathophysiology. One mechanism is that disruption of sleep may lead to a decision to void. Pressman et al⁸ showed that most awakenings from sleep attributing feeling the urge to urinate were a result of sleep disorders, particularly OSAS. But this theory does not explain the nocturnal polyuria. Another mechanism by which OSAS develops nocturia and nocturnal polyuria is thought to be the existence of an increasingly negative intrathoracic pressure caused by partial or complete occlusion of the airway. Each diaphragmatic contraction against obstruction results in a corresponding pulse of negative thoracic pressure and positive abdominal pressure. This stimulates venous return to the atrium and gives a false fluid overload signal. Together with the also developing hypoxemia this results in an increased atrial natriuretic peptide (ANP) secretion.⁹ ANP acts on the kidney to increase sodium and water excretion (natriuresis) and leads to the nighttime polyuria responsible for the nocturia. Furthermore, there are age-related changes in sleep depth and continuity and age-related changes in circadian rhythm amplitude that may contribute to nocturia.¹⁰

One treatment of OSAS is continuous positive airway pressure (CPAP) and thereby it is possible that it can reduce nocturia in these patients provided that no other physiological cause contributed to nocturia. CPAP is effective in reducing symptoms of sleepiness and improving quality of life (QoL) measures in people with moderate and severe OSAS.¹¹

In lower urinary tract symptoms (LUTS), consisting of voiding, postvoiding, and storage symptoms (including nocturia), nocturia is consistently reported to be one of the most bothersome symptoms by male as well as female.¹²

Despite the bother experienced by patients, nocturia is an underreported condition and therefore, the true extent of the problem in the population may be underestimated. As nocturia is underreported, the true incidence of nocturia in the population and more specifically in patients suffering from OSAS is likely to be higher.

The primary aim of this study was to assess the prevalence of nocturia in patients with OSAS who received CPAP. Furthermore, sex differences and QoL were investigated as well.

2 | METHODS

All patients who were referred to the pulmonology department of a large teaching hospital in the Netherlands

and received a CPAP mask for OSAS during 1 year (2014–2015) (N = 368) were invited for a telephone interview regarding nocturia and QoL related to micturition. All patients were interviewed about their nocturia episodes prior to and after CPAP. The interviews were conducted in 2016 cross-sectionally after informed consent was provided. Interviewees underwent at least 1 year of CPAP treatment. Study data were gained from the interview as well as medical records. Following the nature of this study and the rules of the Dutch Central Committee on Research involving Human Subjects (CCMO), central approval of an ethics committee was not required to conduct the study. Local approval was gained by the hospital board.

OSAS was defined as a breathing disorder in which a person frequently stops breathing during his or her sleep and results from an obstruction of the upper airway that occurs because of the inadequate motor tone of the tongue and/or airway dilator muscles. Nocturia has been defined by the International Continence Society as “the need to void one or more times during the night, with each void preceded and followed by sleep.”¹³ A more clinically relevant definition of nocturia is “≥2 voids per night” as at this point it would become bothersome for most individuals.^{14,15} In descriptive analysis, the following information was taken into account: baseline characteristics (age, sex, concomitant diseases, medication use, medical history, and use of CPAP), nocturia (number of nocturnal voids before CPAP, number of nocturnal voids after CPAP, difference in number of nocturnal voids before and after CPAP), and QoL regarding micturition (QoL before CPAP [good-fair-poor], QoL after CPAP [good-fair-poor], difference in QoL before and after CPAP).

Statistical analysis was performed using IBM SPSS statistics 23.0. Continuous data were presented as mean (\pm SE) or median (interquartile range [IQR]). Categorical data were presented as numbers (percentages). Statistical differences were assessed by the Student *t* test for continuous outcomes and by χ^2 tests for categorical outcomes. In case the number of expected patients was too low to conduct the χ^2 test, the likelihood ratio was used. A $P < .05$ was deemed as a statistically significant difference.

3 | RESULTS

Of the 368 patients who were called, 285 patients, (198 male and 87 female) were reached and gave consent to take part in our study. We obtained the requested data from 274 people (190 male and 84 female). The mean age of the interviewed population at that time was 60.3 years (SE = 0.7). Analyzing the different age groups, there are statistically significant ($P = .011$) more men with OSAS in

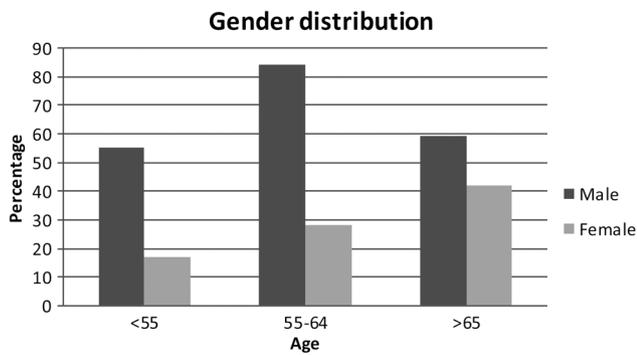


FIGURE 1 Gender distribution of OSAS by age

each group; see Figure 1. Furthermore, there is a peak incidence of OSAS in male between 55 to 64 years old. In the female the increase is gradual as the age increases. There was not a statistically significant difference with respect to the prevalence of nocturia between the sexes prior ($P = .936$) or after CPAP treatment ($P = .398$); see Table 1. Furthermore, no difference was observed with regard to QoL before and after CPAP treatment (with respectively $P = .257$ and $P = .664$).

In the interviewed population 42% experienced some LUTS prior to CPAP treatment. An overview of these

TABLE 1 Gender differences in nocturia and related QoL

Nocturia frequency before CPAP	Male	%	Female	%
0-1	51	26.3	23	26.7
≥2	143	73.7	63	73.3
Total	194	100	86	100
Nocturia frequency after CPAP	Male	%	Female	%
0-1	89	46.8	44	52.4
≥2	101	53.2	40	47.6
Total	190	100	84	100
Rating QoL before CPAP	Male	%	Female	%
Good	128	72.3	53	67.1
Fair	30	16.9	20	25.3
Bad	19	10.7	6	7.6
Total	177	100	79	100
Rating QoL after CPAP	Male	%	Female	%
Good	160	90.4	67	87
Fair	16	9	9	11.7
Bad	1	0.6	1	1.3
Total	177	100	77	100

Abbreviations: CPAP, continuous positive airways pressure; QoL, quality of life.

LUTS is summarized in Table 1. In Table 2 micturition-related medication is shown before and after CPAP treatment. Few differences in medication use were seen before and after treatment with CPAP (Table 3).

Sixty-four patients (23.4%) reported to have had no nocturia episodes before CPAP, 210 patients (76.6%) reported one or more nocturia episode(s). The distribution of the nocturia frequency is shown in Table 4. It is obvious that after starting with CPAP the nocturia frequency has decreased over the entire range. Excesses, in particular, have been reduced and the nocturia frequency has been reduced to a maximum of 4 times instead of 7. Overall 116 (42.3%) patients have experienced a decrease in voids. Furthermore, 200 (73.0%) patients had a clinically relevant (≥ 2 voids per night) nocturia. The median nocturia frequency before CPAP was 3 (IQR = 3). After treatment with CPAP, the number of patients with clinically relevant nocturia was 141 (51.5%). The median nocturia frequency after CPAP was 2 (IQR = 2). The mean reduction of nocturia after starting treatment with CPAP was -1.09 with a standard deviation of 1.58 (P -value one-sample t test: $<.001$).

Analyzing the effects of the treatment on the QoL regarding micturition, we noticed a statistically significant ($P < .001$) improvement of the QoL after the treatment; see Table 4.

Two hundred seventy patients were asked whether medical help was sought for nocturia. This was only the case with 36 people (13.3%). In 193 interviewees, it was possible to find out the reason for not seeking medical help for this complaint. By far the largest group, 109 interviewees (56.5%) experienced no complaints, 42 patients (21.8%) did not experience the nocturia as annoying and 15 patients (7.8%) were assuming that it is normal to void at night. The remaining group indicated a wide range of reasons for not requesting medical assistance.

4 | DISCUSSION

The results of this study show that more than three-quarters of patients with OSAS suffer from nocturia. In our study, it was noticeable that few patients seek medical help for this problem. Many of those interviewed did not see it as a complaint or assumed it was normal. A study by Oelke et al¹⁶ recently found that nocturia is an underreported, undertreated, and poorly managed medical and social problem in adults. In this study, it was found that the total time from the first symptom appearance to first prescribed treatment was approximately 2 years. This suggests that physicians may underestimate the symptom burden and decreased QoL associated with nocturia. Our results indicate that also patient awareness is necessary in recognizing nocturia as a problem. In

TABLE 2 LUTS before CPAP treatment

LUTS specification	Frequency	%	Valid %
Nocturia	31	10.9	29.2
LUTS not specified	28	9.9	26.4
LUTS for which TURP	15	5.3	14.2
Urge	11	3.9	10.4
Nighttime incontinence	10	3.5	9.4
Incontinence not specified	7	2.6	6.5
Chronic residue	3	1.1	2.8
Stress urinary incontinence	1	0.4	0.9
	106	37.2	100

Abbreviations: CPAP, continuous positive airways pressure; LUTS, lower urinary tract symptoms; TURP, transurethral resection of the prostate.

addition, nocturia has been identified as an independent predictor for severe OSAS.^{17,18} Yamamoto et al¹⁹ looked at the prevalence of OSAS among patients that visited a urology clinic complaining of nocturia. They reported that OSAS is as prevalent in patients who visit a urology clinic complaining of nocturia as in those who visit a sleep apnea clinic. Of the 34 patients who also had consulted a urologist, 70% had more than mild OSAS. Because many patients seek help for nocturia instead of OSAS further study of patient characteristics is necessary to identify the patients with OSAS in particular because the cause of nocturia is multifactorial.

In this study, 42.3% of all patients treated with CPAP, experienced a reduction of nocturia with one or more voiding episodes per night. Although the limitation of this study is its retrospective nature it shows significant improvement of nocturia and QoL. In this study, we used

TABLE 3 Use of medication before and after treatment

Medication	Frequency pre CPAP	%	Frequency after CPAP	%
No urinary-related medication	203	71.2	215	75.4
Not clear	22	7.7	10	3.5
Urinary-related medication	19	6.7	16	5.6
Mirabegron	1	0.4	4	1.4
Anticholinergic	4	1.5	4	1.5
Diuretics	17	2.5	16	5.6
Alfa blocker	1	0.4	1	0.4
	267	93.7	266	93.3

Abbreviation: CPAP, continuous positive airways pressure.

TABLE 4 Reduction of clinically significant nocturia and effect of CPAP on QoL regarding micturition

Nocturia frequency	Before CPAP	%	After CPAP	%
0-1	74	26	133	48.5
≥2	206	72.3	141	51.5
Total	280		274	
Missing	5		11	
Rating QoL	Before CPAP	%	After CPAP	%
Good	181	70.7	227	89.4
Fair	50	19.5	25	9.8
Bad	25	9.8	2	0.8
Total	256	100	254	100
Missing	29		31	

Abbreviations: CPAP, continuous positive airways pressure; QoL, quality of life.

the definition of bothersome nocturia (“≥2 voids per night”) which is at least arbitrary. The first interrupted sleep period may be more useful in future analysis to measure the effect on sleep quality.²⁰

CPAP is effective in reducing symptoms of sleepiness and improving QoL measures in people with moderate and severe OSAS.¹¹ CPAP also seems to be effective in reducing the frequency of nocturia and the associated nighttime polyuria.²¹ In a meta-analysis by Wang et al,²² it was concluded that CPAP possibly is an effective treatment for reducing nocturia associated with OSAS and improves the QoL in these patients. At this time CPAP is not the only treatment option in OSAS and the effect of other treatment options like lifestyle changes, oral devices, and surgical procedures must also be evaluated.

We did see that the prevalence of OSAS in men is more concentrated in the age category between 55 and 65 years while in women the increase is gradual as they age. A possible explanation lies in the relationship between lifestyle factors and OSAS. In women, it appears to be mainly caused by aging. The clinical consequence could be that clinicians are more alert in diagnosing OSAS in a middle-aged man when nocturia is the main complaint. Furthermore, studies on lifestyle interventions may give rise to better treatment options in patients with nocturia caused by OSAS.

5 | CONCLUSION

The prevalence of nocturia in patients diagnosed with OSAS is 75.8% in both males and females. There were no statistically significant sex differences. Although arbitrary, a nocturia frequency of 2 or more is found to be bothersome

and is therefore called clinically relevant, and is prevalent in almost three-quarters of all patients. This study also provides an indication for more research into recognizing the nocturia as a symptom by patients so that help is sought more and more quickly. After treatment with CPAP, almost half of the patients experienced a decrease in the nocturia frequency of one or more voids. Clinically relevant nocturia was reduced with one-third after CPAP. CPAP not only reduced the number of voids during the night but also improved the associated QoL. Almost no one scored bad after treatment.

This study shows that there is a relation between nocturia and OSAS and this should prompt the urologist to think outside of the “urology box.” The multifactorial nature of Nocturia deserves often a multidisciplinary approach and in the case of OSAS referral to a pulmonologist and treatment of these patients with CPAP can relieve symptoms in almost half of patients and treatment with CPAP shows a clear improvement in the QoL.

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