A person with nocturia awakens one or more times to urinate during a sleep period. Nocturia is difficult to treat because it typically occurs in conjunction with other disorders. Undiagnosed obstructive sleep apnea (OSA) can contribute to nocturia. However, physicians often do not ask patients complaining of nocturia about symptoms of OSA. This oversight may contribute to difficulties in treating nocturia.

Nocturia may be caused by lower urinary tract disorders (e.g., enlarged prostate, overactive bladder, cystitis [bladder inflammation]); systemic disorders (e.g., congestive heart failure, diabetes, metabolic disorders); kidney disorders (e.g., chronic renal failure); and drugs (e.g., furosemide) or foods (e.g., caffeine, alcohol) that cause diuresis (i.e., induce urination). Alpha-adrenergic blockers and anticholinergic drugs (both of which reduce urine production) may be used to treat nocturia.

The prevalence of nocturia is unclear because few studies have specifically focused on this symptom. One study\(^1\) in 1996 reported a prevalence of 58 percent and 66 percent in women and in men, respectively, who are 50–59 years, and a prevalence of 72 percent and 31.91 percent in women and men, respectively, who are older than 80 years. More recent studies report a prevalence of 11 percent–31 percent.\(^2\)-\(^5\) Some research indicates that the prevalence of nocturia among patients with OSA ranges 40 percent–50 percent (using the criterion of ≥ 2 voids per night).\(^6\)

In OSA, the upper airway muscles relax excessively during sleep, which allows tissues such as the tonsils and adenoids to be drawn into the airway and block airflow. A person makes increasingly strong efforts to breathe as the blood oxygen level falls. The decrease in the oxygen level ultimately triggers a brief arousal. On arousing, the upper airway muscle tone is restored and the airway opens, thereby allowing the person to take a few deep quick breaths to restore the oxygen level. Once the oxygen level is restored, the person resumes sleep, which may set the stage for another apnea event.

Continuous positive airway pressure (CPAP) is used to counteract upper airway collapse in OSA. In this treatment, pressurized air flows through a mask that fits over the nose or nose and mouth into the upper airway, and pushes against upper airway structures to prevent their collapse during sleep. As a result, intermittent collapse and arousals are prevented and a person has more consolidated sleep.

One theory on how OSA may contribute to nocturia focuses on the excretion of atrial natriuretic peptide (ANP), a powerful vasodilator that heart cells release into the bloodstream to reduce high fluid volume in the body.\(^7\) When ANP reaches the kidneys, it inhibits the secretion of renin and aldosterone secretion. This inhibition increases urine production.

During the upper airway blockage in an OSA episode, a person makes increasingly strong efforts to breathe. As the lungs press against the heart with each effort to breathe, the heart erroneously senses that there is an excessive fluid volume. In response to this false signal, the heart cells increase their production of ANP, which may then induce the production of urine and result in nocturia.

Another possibility for the interconnection between OSA and nocturia is the impact of oxidative stress resulting from intermittent episodes of apnea-induced hypoxia. In a study\(^8\) that used a rat model of OSA, the investigators noted increased levels of bladder oxidative stress markers (e.g., malondialdehyde and oxidation protein products), instability of the detrusor muscle (when relaxed this muscle allows the bladder to store urine; it contracts during urination), bladder noncompliance, increased spontaneous bladder contractions, and increased urinary frequency and total urine output in rats exposed to OSA conditions. Oxidative stress may similarly contribute to nocturia in humans, although this factor has not been investigated in depth.

How CPAP treatment improves nocturia in people with OSA is unclear. It may be that CPAP treatment reduces nocturia by impacting the renin–angiotensin–aldosterone system. Renin (pronounced “REE-nin”), angiotensin, and aldosterone are three hormones that work in conjunction (i.e., the renin–angiotensin–aldosterone system) to maintain fluid homeostasis in the body. A disruption in this system can lead to increased urination.

Various researchers have investigated the impact of CPAP
Maeda6 and colleagues. In their study, the researchers investigated nocturia in younger men, as demonstrated in a study by Takahiro. However, some research indicates that CPAP treatment helps of nocturia increases as men age because of prostate enlargement. Many studies that have investigated the beneficial effects of CPAP treatment on plasma levels of renin and aldosterone in men with OSA. The men were divided into the untreated group or CPAP-treated group. For two nights, the plasma levels of renin and aldosterone were measured every 10 minutes. In the CPAP-treated men, Follenius noted diminished excretion of urine, increased plasma volume, a significant increase in the mean levels of plasma renin and aldosterone, and similar plasma renin activity as that of people without sleep apnea. Continuous positive airway pressure treatment also restored the circadian rhythmicity of renin and aldosterone production. Based on these findings, Follenius concluded that apnea-induced sleep disruption was associated with the loss of the circadian rhythmicity of renin production, and that the restoration of the rhythmicity of renin and aldosterone production may contribute to the normalization of urine production after CPAP treatment.

For patients who may be unwilling or unable to tolerate CPAP treatment, some research indicates that nocturia can be improved when apnea is treated by other means. In a recent Korean study, Hyoung Keun Park10 and colleagues found that patients whose OSA was treated by uvulopalatopharyngoplasty (UPPP, a surgery that opens the upper airway by removing the uvula, tonsils, and other upper airway tissues) had fewer nocturia episodes after this surgical treatment. In their study, 66 men with OSA underwent UPPP. The overall success rate of UPPP in their study was 73 percent. Patients were evaluated preoperatively and postoperatively for lower urinary tract symptoms, based on the International Prostate Symptom Score and Overactive Bladder Symptom Score questionnaires. Approximately 53 percent of the patients experienced a significant decrease in the number of nocturia episodes and other urinary symptoms (e.g., overactive bladder). On dividing patients by treatment success or treatment failure (i.e., apnea episodes did not decrease by 50 percent or more), Park noted that the success group had a significant posttreatment decrease in the number of nocturia episodes, whereas the failure group did not. Based on these results, Park concluded that nocturia and other urinary symptoms can be improved by surgically correcting OSA.

Many studies that have investigated the beneficial effects of CPAP treatment on nocturia have focused on older men because the risk of nocturia increases as men age because of prostate enlargement. However, some research indicates that CPAP treatment helps nocturia in younger men, as demonstrated in a study by Takahiro Maeda6 and colleagues. In their study, the researchers investigated the prevalence of nocturia among men with newly diagnosed moderate to severe OSA. They divided the men into two groups by age: < 50 years and ≥ 50 years. Nocturia was defined as ≥ 2 episodes of nighttime urination. (There is some controversy in the literature whether one void is “abnormal”; therefore, some researchers consider two or more voids as “abnormal.”) They found that the severity of nocturia was correlated with the severity of OSA in the younger group (i.e., < 50 years old), compared to the older group (i.e., ≥ 50 years). Treatment by CPAP reduced the number of nocturia episodes in 75 percent of the younger patients and in 90 percent of the older patients. Maeda suggests that, because the number of nighttime urinations can be easily monitored by urologists and general physicians, this symptom may be a useful for screening tool for patients with moderate to severe OSA, especially in patients younger than 50 years old.

To what extent CPAP treatment decreases nocturia episodes is unclear because many studies investigating this have involved a small number of patients.11 With this in mind, Rahnamai12 and colleagues used a large number of participants to assess the incidence of nocturia in CPAP-treated OSA patients. The study involved 256 patients. The patients answered a questionnaire about their nocturia episodes before and after CPAP treatment. The patients were subdivided into seven groups, based on the number of nightly nocturia episodes: (1) no nocturia episodes before or after treatment; (2) one nocturia episode; (3) two nocturia episodes; (4) three nocturia episodes; (5) four nocturia episodes; (6) five nocturia episodes; and (7) seven nocturia episodes. Rahnamai found that the prevalence of nocturia among the patients was 69 percent and that CPAP treatment reduced nocturia episodes in 65 percent of the patients. No patient had an increase in nocturia with CPAP treatment. Rahnamai concluded that a clear relationship exists between OSAS treatment and the reduction of nocturia episodes.

Some studies10,12,13 have included men and women with nocturia and OSA, and report a reduction in nocturia episodes in both sexes when treated for OSA. However, physicians, even those in the field of urology, often do not ask male or female patients complaining of nocturia about symptoms of OSA. This oversight may contribute to the difficulty in relieving nocturia episodes and may lead to a patient being treated for a different problem. For example, some older men may erroneously be treated for prostate enlargement when the nocturia is related to OSA. Physicians need to consider asking patients complaining of nocturia, especially patients who do not have kidney or (in men) prostate problems, about symptoms of sleep apnea (e.g., loud snoring, awakening gasping for air, daytime sleepiness). If a sleep study proves the patient has OSA, then treating it may improve nocturia.
REFERENCES


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