

Chapter 19: Nocturia in Elderly Persons and Nocturnal Polyuria

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Nocturia is defined by the International Continence Society as the interruption of sleep one or more times at night to void.¹ Although nocturia is relatively uncommon among younger adults, by 80 yr of age, the prevalence rises to 80 to 90% in both men and women.² The presence of nocturia disrupts sleep, leading to daytime somnolence, depressive symptoms, cognitive dysfunction, and a reduced sense of well being and quality of life.³ Moreover, nocturia is associated with an increased risk morbidity and even mortality.^{4,5}

PATHOPHYSIOLOGY

Although it is commonly assumed that nocturia in the elderly is primarily a urologic problem, such thinking is inaccurate. The pathophysiology of nocturia in the elderly involves the complex interplay of several factors.⁶ Age-related changes in the urinary system and in renal function occur. Sleep itself has effects on renal function. Sleeping patterns and sleep architecture change with aging. Finally, disease states and medications may affect the urinary system, sleep architecture, and renal function. Common causes of nocturia in the elderly are listed in Table 1.

SYNDROME OF NOCTURNAL POLYURIA

Nocturnal polyuria is a syndrome where the usual day to night ratio of urine production is altered.⁷ In patients with nocturnal polyuria, >33% of the total daily urine output occurs at night, although the daily total urine output remains normal. A careful voiding diary, incorporating measurements of voided volumes, is essential to make the diagnosis. Common causes of nocturnal polyuria are listed in Table 2.

Conditions such as congestive heart failure, nephrotic syndrome, autonomic neuropathy, and venous insufficiency lead to interstitial edema formation during the day. Mobilization of the accumulated interstitial fluid while recumbent results in nocturia. Obstructive sleep apnea is associated with excessive atrial natriuretic peptide production. Neurologic diseases, such as Alzheimer's disease and Parkinson's disease, are associated with alterations in the diurnal secretory pattern of neurohormones, such as natriuretic peptides and anti-diuretic hormone. Patients with chronic kidney disease are unable to maximally concentrate their urine and often must void at night.

In many cases, the cause of nocturnal polyuria is undefined. In idiopathic nocturnal polyuria, Asplund and Aberg⁸ suggested that anti-diuretic hormone (ADH) levels, which are typically elevated during sleep, are abnormally low in these individuals. This finding is not universally seen, however, particularly among women.⁹ Furthermore, a relative nocturnal deficiency of ADH fails to explain the altered diurnal excretion patterns of sodium and nonelectrolyte solutes that occur among these individuals. In some individuals with nocturnal polyuria, diurnal variation in GFR is absent or even reversed, such that creatinine and sodium excretion rates are higher at night than during the day.¹⁰ Some investigators suggest that these increases are associated with higher night-time BP or the "nondipping" phenotype.¹¹

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Table 1. Common causes of nocturia in the elderly

Bladder dysfunction
Bladder outlet obstruction (caused by, for example, benign prostatic hyperplasia)
Severe detrusor dysfunction/large residual urine volume
Detrusor overactivity
Urinary tract infection
Decreased functional bladder capacity
Bladder tumor or bladder stones
Pelvic floor laxity (caused by, for example, cystocele, uterine prolapse)
Excessive nocturnal urine production
Edema-forming states (e.g., congestive heart failure, nephrosis)
Obstructive sleep apnea
Neurodegenerative conditions (e.g., Parkinson's disease, Alzheimer's disease)
Diabetes mellitus and diabetes insipidus
Hypokalemia and hypercalcemia (causing nephrogenic diabetes insipidus)
Drugs (diuretics, calcium channel blockers, caffeine, alcohol, SSRI)
Chronic kidney disease
Autonomic neuropathy and venous stasis
Excessive fluid intake
Idiopathic nocturnal polyuria (possibly caused by deficient nocturnal ADH secretion)

EVALUATION

The evaluation of a patient with nocturia is outlined in Table 3. A careful history and physical examination provide clues to the etiology of nocturia. A weakened urinary stream, hesitancy, and a sense of incomplete voiding suggest bladder outlet obstruction. Frequency, urgency, and bladder spasms suggest bladder irritation, perhaps caused by infection. Gross hematuria might indicate a bladder tumor or stones. The presence of concurrent diseases and the use of medications such as diuretics, calcium channel blockers, and selective serotonin reuptake inhibitors (SSRIs), and habits such as excessive intake of fluids, alcohol, and caffeine are also important to note.

On physical examination, orthostatic vital signs should be assessed. Evidence of edema-forming states, including venous insufficiency, should be sought. Abdominal examination and a careful genitourinary examination should be performed to detect prostatic enlargement in men, pelvic floor laxity in women, bladder outlet obstruction—as manifest by a large postvoid residual urine volume—or evidence of neurologic

Table 2. Causes of the syndrome of nocturnal polyuria

Congestive heart failure
Obstructive sleep apnea
Nephrotic syndrome
Autonomic neuropathy
Chronic kidney disease
Venous insufficiency
Neurologic diseases (Parkinson's disease, Alzheimer's disease)
Idiopathic

Table 3. Evaluation of nocturia in the elderly

History: including medications, comorbid conditions
Physical examination: orthostatic vital signs, complete exam including abdominal and genitourinary exams
Laboratory studies: electrolytes, calcium, renal function, glucose, urinalysis
Other studies: post void residual volume, urinary flow studies, voiding diary
Other studies to be considered: urine culture, polysomnogram, 24-h ambulatory blood pressure monitor, urodynamic evaluation

deficits related to the sacral nerve roots, including sensory deficits, poor sphincter tone, or absent anal wink reflex.

Initial laboratory testing should include assessment of renal function, blood glucose and electrolytes, serum calcium, and urinalysis (incorporating microscopic examination of the urine). If symptoms suggest infection, a urine culture should be obtained. Urinary flow rate and postvoid residual urine volume should also be assessed. The patient should be requested to keep a careful voiding diary for 3 d. The volume and time of each void, as well as whether or not the voiding episode disrupted sleep, should be noted. If bladder dysfunction or bladder outlet obstruction is suspected, detailed urodynamic evaluation may be indicated. A polysomnogram may be indicated if symptoms suggest obstructive sleep apnea. A 24-h ambulatory BP recording can be considered to ascertain the presence of nondipping at night.

TREATMENT OF NOCTURIA IN THE ELDERLY

Treatment for nocturia in the elderly is outlined in Table 4. Simple maneuvers, such as reducing fluid intake for 6 h before recumbency, are usually not successful. Compression stockings, phototherapy, and pelvic floor exercises can be tried. Phototherapy is thought to reset the normal circadian rhythm

Table 4. Treatment of nocturia in the elderly

Nonpharmacologic
Reducing fluid intake 6 h before recumbency
Reduce caffeine and alcohol intake
Dried fruit
Compression stockings
Biofeedback, bladder/pelvic floor exercises
Phototherapy
Continuous positive airway pressure (for obstructive sleep apnea)
Neuromodulation
Pharmacologic
Alpha adrenergic blockers, 5- α -reductase inhibitors
Estrogen creams, hormone replacement
Nonsteroidal anti-inflammatory agents
Melatonin
Imipramine
Anticholinergic agents
Loop diuretics
Desmopressin

that is disrupted in patients with nocturia. Continuous positive airway pressure for obstructive sleep apnea improves nocturia in anecdotal cases.

Double-blind, placebo-controlled studies have been performed examining various pharmacologic measures in the treatment of nocturia. Most of the studies are small and are of short-term duration. The administration of loop diuretics timed 6 to 10 h before recumbency, which induces a mildly hypovolemic state, can be tried but is usually not successful. The most extensive studies have been performed using desmopressin, a synthetic analog of anti-diuretic hormone. Multi-center, double-blind, placebo-controlled trials of oral desmopressin in both men and women have shown a reduction in nocturnal voiding among patients with nocturnal polyuria during a 10- to 12-mo follow-up.¹² Adverse effects—headache, nausea, dizziness, and peripheral edema—were seen in <5 to 10% of cases. Hyponatremia was seen in 14% of patients but was asymptomatic and mild in most cases. Although adverse effects seen in these trials were few, several anecdotal cases of severe symptomatic hyponatremia with desmopressin have since been reported especially when used in the elderly. In December 2007, the FDA issued a warning on the use of desmopressin.¹³

In those who fail pharmacologic therapy, electrical neuro-modulation of the sacral nerves using either transcutaneous or implantable electrodes has been used in patients with detrusor overactivity with some success.¹⁴

CONCLUSIONS

Nocturia in the elderly is a common condition associated with increased morbidity and mortality. Nocturia results from the complex interplay of age-related changes in the urinary system, renal function, sleeping patterns, concurrent disease states, habits, and medications. Appropriate treatment requires identifying the correct underlying pathophysiologic cause of nocturia in a given patient. The syndrome of nocturnal polyuria, a frequent cause of nocturia among the elderly, may result from decreased nocturnal secretion of antidiuretic hormone. Several treatment options are available for nocturia in the elderly, depending on the underlying cause.

TAKE HOME POINTS

- Nocturia is a common condition in individuals >60 yr old and is associated with morbidity and mortality

- Voiding diaries are essential for diagnosis
- Consider alternative diagnoses
- Management of nocturia is frequently nonsurgical
- Several therapeutic options are available

DISCLOSURES

None.

REFERENCES

*Key References

1. van Kerrebroeck P, Abrams P, Chaikin D, Donovan J, Fonda D, Jackson S, Jennum P, Johnson T, Lose G, Mattiasson A, Robertson G, Weiss J; Standardisation Sub-committee of the International Continence Society: The standardisation of terminology in nocturia: report from the standardisation sub-committee of the International Continence Society. *Neurourol Urodyn* 21: 179–183, 2002
2. Weiss J: Nocturia. *J Urol* 163: 5–12, 2000*
3. Coyne K, Zhou Z, Bhattacharyya S, Thompson C, Dhawan R, Versi E: The prevalence of nocturia and its effect on health-related quality of life and sleep in a community sample in the USA. *BJU Int* 92: 948–954, 2003
4. Stewart R, Moore M, May F, Marks R, Hale W: Nocturia: a risk factor for falls in the elderly. *J Am Geriatrics Soc* 40: 1217–1220, 1992
5. Asplund R: Mortality in the elderly in relation to nocturnal micturition. *Br J Urol Int* 84: 297–301, 1999
6. Kujubu DA, Aboseif SR: An overview of nocturia and the syndrome of nocturnal polyuria in the elderly. *Nature Clin Prac Nephrol* 4: 426–435, 2008*
7. Asplund R: The nocturnal polyuria syndrome. *Gen Pharmacol* 26: 1203–12309, 1995*
8. Asplund R, Aberg H: Diurnal rhythm of antidiuretic hormone in elderly subjects with nocturia. *Med Sci Res* 19: 765–766, 1991*
9. Asplund R, Aberg A: Diurnal variation in the levels of antidiuretic hormone in the elderly. *J Int Med* 229: 131–134, 1991
10. Fujii T, Uzu T, Nishimura M, Takeji M, Kuroda S, Nakamura S, Inenaga T, Kimura G: Circadian rhythm of natriuresis is disturbed in nondipper type of essential hypertension. *Am J Kidney Dis* 33: 29–35, 1999
11. Graugaard-Jensen C, Rittig S, Djurhuus J: Nocturia and circadian blood pressure profile in healthy elderly male volunteers. *J Urol* 176: 1034–1039, 2006
12. Lose G, Mattiasson A, Walter S, Lalos O, van Kerrebroeck P, Abrams P, Freeman R: Clinical experiences with desmopressin for long-term treatment of nocturia. *J Urol* 172: 1021–1025, 2004*
13. Alert: Information for healthcare professionals: desmopressin acetate (marketed as DDAVP nasal spray, DDAVP rhinal tube, DDAVP, DDVP, Minirin, and Stimat nasal spray). Available online at: <http://www.fda.gov/CDER/DRUG/infoSheets/HCP/desmopressinHCP.htm>.
14. Hassouna MM, Siegel SW, Njeholt AA, Elhilali MM, van Kerrebroeck PE, Das AK, Gajewski JB, Janknegt RA, Rivas DA, Dijkema H, Milam DF, Oleson KA, Schmidt RA: Sacral neuromodulation in the treatment of urgency-frequency symptoms: a multicenter study on efficacy and safety. *J Urol* 163: 1849–1854, 2000

REVIEW QUESTIONS: NOCTURIA IN ELDERLY PERSONS AND NOCTURNAL POLYURIA

1. Which of the following is most correct regarding nocturia in the elderly?
 - a. The majority of cases are due to urologic issues
 - b. It disrupts quality of life but has no effects on morbidity or mortality
 - c. Its prevalence increases to 80 to 90% among those 80 yr old and older
 - d. Chronic kidney disease is associated with decreased urine output
2. Which of these is NOT associated with nocturia in the elderly?
 - a. Detrusor overactivity
 - b. Hypercalcemia
 - c. Neurodegenerative conditions
 - d. Syndrome of inappropriate antidiuretic hormone
3. Which of the following is most correct regarding the syndrome of nocturnal polyuria?
 - a. Oral loop diuretics taken 6 to 10 h before recumbency reduce nocturnal urinary frequency
 - b. Nocturnal antidiuretic hormone secretion is decreased in all cases
 - c. Oral desmopressin is both ineffective and potentially dangerous
 - d. Continuous positive airway pressure (CPAP) may help obstructive sleep apnea but has no effect on nocturnal polyuria
4. All of the following are causes of the syndrome of nocturnal polyuria EXCEPT:
 - a. Congestive heart failure
 - b. Venous insufficiency
 - c. Autonomic dysfunction
 - d. Acute use of nonsteroidal anti-inflammatory drugs
5. All of the following treatment options have been used for nocturia in the elderly EXCEPT:
 - a. Neuromodulation
 - b. Phototherapy
 - c. Biofeedback
 - d. Calcium channel blockers