

## CLINICAL VIGNETTE

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# Nocturnal Polyuria Syndrome in the Elderly

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### *Case Report*

An 87-year-old female with hypertension, venous insufficiency with chronic edema, and chronic kidney disease, was hospitalized for hip fracture and discharged to a skilled nursing facility (SNF) for rehabilitation. The patient has also been grieving over the loss of her spouse and was recently started on treatment for depression with escitalopram. During her stay at the SNF, she complained of increased urinary frequency, only at night. She denied urinary symptoms during the day and denied drinking more fluids or caffeine products. Urine culture was negative for infection, post void residuals were normal and there were no issues with incontinence. Her symptoms persisted and continued to be bothersome only at night. She saw urology and workup was overall negative for any bladder or urologic abnormalities. She was diagnosed with a condition called nocturnal polyuria syndrome, where urinary frequency only occurs at night and is not associated with infection or other genitourinary pathology. She was predisposed from her chronic conditions of venous stasis and kidney disease, and her symptoms were exacerbated by her recent hip fracture, decreased mobility with prolonged recumbent state, and the start of an anti-depressant for her mood. Her symptoms improved with bladder training and regular voiding, reducing fluid intake before bedtime, and improving control of her venous stasis and chronic kidney disease. Although she continued to have some symptoms, they were less bothersome, and she adjusted to a new baseline.

### *Discussion*

Nocturia is defined as the need to wake and pass urine at night. In the elderly, nocturia includes a broad differential and is often not primarily a urologic problem. It involves a complex combination of factors that is affected by age-related changes, renal function, chronic medical diseases, sleep patterns and medications. Nocturia can occur as a consequence of either, decreased bladder capacity and bladder dysfunction or from excessive nocturnal urine production. Examples of bladder dysfunction include bladder outlet obstruction, detrusor hyperactivity, pelvic floor laxity, bladder tumors and bladder infections. Some conditions that produce excessive nocturnal urine include congestive heart failure, obstructive sleep apnea, neurodegenerative conditions, medications, kidney disease, venous stasis, autonomic neuropathy, and idiopathic causes from decreased nocturnal anti-diuretic hormone (ADH) secretion.<sup>1</sup> In general, the elderly are more predisposed to nocturnal ADH deficiency.<sup>2</sup>

The syndrome of nocturnal polyuria or nocturnal urine overproduction is common in patients with nocturia and may be associated with higher morbidity and mortality.<sup>1</sup> It involves change in the day to night ratio of urine production.<sup>2</sup> Over 1/3 of the total daily urine output happens at night while the daily urine output is within normal amounts and frequency. The mechanism behind nocturnal polyuria is still unclear, but this condition may be related to a deficient level of anti-diuretic hormone (ADH) at night, when they typically should be increased.<sup>2,3</sup> In some cases, there is a lack of diurnal changes in GFR and creatinine and sodium excretion rates are elevated at night compared to the day.<sup>4</sup>

The medical conditions that produce excessive nocturnal urine increase the likelihood for this syndrome. It is felt that edema-inducing states such as heart failure and venous insufficiency cause increased interstitial fluid formation and retention during day. Mobilization of the accumulated fluid while lying recumbent at night also results in increased nocturnal urination. Those with chronic kidney disease have less ability to effectively concentrate urine, which can lead to the urgency to void at night. Other conditions such as obstructive sleep apnea or neurologic disease cause excessive atrial natriuretic peptide production or alternations in neuro-hormone secretions, resulting in increased nocturia.

There is also a unique relationship between nocturnal polyuria and depression. Major depression is associated with an increase in nocturia, up to 6 fold in men and 3 in women.<sup>5</sup> The underlying mechanism is disrupted anti-diuretic hormone secretion at night and decreased nocturnal bladder capacity from the central and peripheral serotonergic mechanisms.<sup>2,3</sup> In patients with depression, the production and release of ADH in the hypothalamus is reduced, which also can be responsible for maintaining the circadian rhythm.<sup>6,7</sup> Sleep deterioration is common in patients with major depression, and sleep disturbance increases nocturnal urinary output.<sup>8</sup>

When evaluating a patient, it is important to obtain a thorough history and physical including a focus on urinary complaints (i.e., asking about incomplete voiding, weakened urinary stream, hesitancy, frequency, urgency). Detailed past medical history of chronic diseases can help identify risk factors and predisposing conditions.

Medications such as diuretics, selective serotonin reuptake inhibitors (SSRIs) can increase the risk for nocturia. Excessive

fluid intake, alcohol or caffeine use can also increase urine production. Physical exam should evaluate cardiovascular, pulmonary, abdominal and genitourinary systems. Laboratory testing should include renal function, electrolytes, and urine analysis and culture, if infection is suspected. A voiding diary can be helpful to track urinary symptoms and patterns. Also if bladder dysfunction is suspected, urodynamic studies may be useful.

Treatment options for nocturnal polyuria are broad. In general, conservative, non-pharmacologic measures are initially advised. Examples include limiting fluid intake several hours before bedtime, using compression stockings for venous insufficiency and pelvic floor exercises for pelvic floor dysfunction. Restoring proper sleep/wake cycles and circadian rhythms can also improve sleep patterns and in turn, reduce nocturia. It is important to treat the underlying medical conditions, optimize management of symptoms and minimize hypervolemic states.

Regarding medication options, the most extensive studies have been performed with desmopressin, a synthetic analog of antidiuretic hormone. Several double blinded, placebo-controlled trials using oral desmopressin have shown decrease in nocturnal polyuria over 10-12 month follow-up period.<sup>9</sup> However, side effects can include nausea, dizziness, headaches and peripheral edema in <10% of cases. Also, hyponatremia can develop. Although generally mild, rare cases of severe symptomatic hyponatremia have been reported, the FDA issued a warning on the use of desmopressin in 2007.<sup>10</sup>

In this case, the patient became symptomatic with nocturnal polyuria after her hip fracture. She was predisposed with her underlying medical conditions of kidney disease and venous stasis and her symptoms were exacerbated by her prolonged immobility and depression after the loss of her husband. The initiation of an SSRI likely precipitated further disruption of the ADH regulatory response, with lower ADH secretion levels at night, causing her nocturia to be more prominent. Her symptoms persisted, but improved with conservative management, and became more tolerable over time.

### Conclusion

Nocturnal polyuria can be noted in the elderly and is associated with higher morbidity and mortality. The etiology is often multifactorial and involves an interplay of age-related conditions, although the exact mechanism is still unclear. Risk factors include the medical conditions and can be affected by medications, habits, and sleeping patterns. Other cases are idiopathic and the pathophysiology may be due to decreased anti-diuretic hormone secretion at night reflecting an alteration in the circadian rhythm. This impairs proper renal concentration and increases nocturnal urinary output. Treatment should start with conservative options and addressing the underlying concurrent diseases. If medication is needed, desmopressin has been shown to be effective in numerous studies, but can be associated with side effects and has an FDA warning for severe hyponatremia.

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