183 Nocturia

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Definition

Nocturia, the awakening from sleep at night to pass urine, is often an early and subtle clue to important systemic disease. It is usually due to the loss of ability to elaborate a concentrated urine of low solute content in the nighttime hours.

Technique

Ask the patient if he arises from sleep to urinate or "pass water," and if so, how many times and how much (i.e., a few drops or a few cupfuls). Determine whether the patient then drinks a glass of water and whether it is because of thirst or from habit. Does the patient ordinarily drink tea, coffee, or other beverages in the evening? If not previously elicited, a history of stones, recurrent urinary tract infections, or pelvic surgery may be sought at this point.

Basic Science

Urine volume or flow rate is determined by solute load, osmolality of medullary interstitium, and response to vasopressin. In the normal circumstance, sodium, potassium, and chloride excretion are high during the day and low at night. Plasma vasopressin levels are higher at night than in the day. Thus we excrete most of our solute load, especially electrolytes, during the waking hours and elaborate a concentrated acid urine of low solute content overnight. Loss of the diurnal variation of solute excretion or the ability to raise the urine osmolality above plasma will result in increased nocturnal urine flow without an obvious increase in daytime urine volume. Even with isosthenuria, the normal daily solute load of 450 to 750 mOsm will be excreted in 1500 to 2500 ml of urine. In contrast, the absence of vasopressin effect will result in persistent hyposthenuria (water diuresis) and cause daytime polyuria as well as nocturia. Similarly, a substantial increase in solute excretion will cause daytime polyuria with nocturia (Table 183.1).

Clinical Significance

Nocturia without Polyuria

Clinical conditions associated with the loss of normal diurnal variation in solute excretion or loss of renal concentrating ability result in nocturia without polyuria. Patients with congestive heart failure have decreased renal plasma flow and increased filtration fraction during ambulation. This is associated with sodium retention. Nighttime recumbency improves renal hemodynamics and sodium excretion, resulting in nocturia. This may be an early manifestation of heart failure, occurring in the preedematous stage. Similar improvement in renal hemodynamics with recumbency accounts for the nocturia that accompanies cirrhosis with ascites and the nephrotic syndrome.

The nocturia of chronic renal disease has been traditionally attributed to the early loss of concentrating ability that accompanies most renal disease regardless of etiology. Careful analysis of excretory patterns of patients with chronic renal disease reveals the principal cause of the nocturia to be increased nocturnal solute excretion. A similar nocturnal saluresis in some renal transplant recipients accounts for the nocturia that may persist for up to a year after transplantation.

A recent finding in the healthy elderly population is that 70% have nocturia, 40% twice a night or more. This is, once again, due to loss of the normal diurnal variation in solute excretion.

The administration of beta-adrenergic blocking drugs reverses the normal day–night pattern of sodium excretion. The effect is most pronounced in people with incipient or

Table 183.1
Nocturia

Nocturia without polyuria
Loss of normal diurnal variation in solute excretion
Edema-forming states: congestive heart failure, cirrhosis, nephrotic syndrome
Chronic renal disease; postrenal transplantation
Advanced age
Drugs: β-adrenergic blockage, diuretics
Loss of renal-concentrating ability
Chronic renal disease
Malnutrition
Nocturia with polyuria
Water diuresis
Pituitary diabetes insipidus
Nephrogenic diabetes insipidus
Hereditary
Electrolyte abnormality: hypercalcemia, hypokalemia
Tubule interstitial disease: medullary cystic disease, analgesic nephropathy, obstructive nephropathy, sickle cell disease, pyelonephritis
Drugs: lithium, amphotericin B, demethylchlortetracycline, methoxyfluorane
Psychogenic water drinking
Solute diuresis
Endogenous
Glycosuria: uncontrolled diabetes mellitus
Urea: hypercatabolic states
Exogenous
Hypertonic glucose, saline, mannitol, radiocontrast media
Combined water and solute diuresis
Postobstructive diuresis
Recovery phase of acute tubular necrosis
Early postrenal transplantation

overt heart failure, but has a lesser effect in normal individuals as well. It may result in nocturia. Diuretics with a long duration of action (chlorthalidone) or potent short-acting diuretics (furosemide) taken shortly before bedtime will effect a nocturnal sodium diuresis.

Loss of maximal urinary concentrating ability occurs early in all forms of renal diseases, especially those affecting medullary structures preferentially. This loss of concentrating ability contributes to the nocturia of chronic renal disease. Urea is an important constituent of a normal hypertonic medullary interstitium. The malnourished patient may have insufficient intramedullary urea to effectively concentrate the urine, and nocturia results.

Nocturia with Polyuria

Loss of urinary concentrating ability alone will not cause urine volumes in excess of 2500 ml/day. However, either the absence of a vasopressin effect with persistent hyposthenuria (water diuresis) or an increased solute load (solute diuresis) results in urine flows in excess of 3000 ml/day. These patients have daytime frequency as well as nocturia.

Central or pituitary diabetes insipidus causes a partial or complete absence of vasopressin. It may be congenital or may be caused by a wide variety of surgical, traumatic, inflammatory or vascular conditions. Administration of vasopressin restores the ability to concentrate the urine with a prompt reduction in urine flow. Nephrogenic diabetes insipidus, the lack of renal response to circulating or administered vasopressin, also occurs in a wide variety of circumstances. Hereditary nephrogenic diabetes insipidus is transmitted as a sex-linked recessive trait. Because it is difficult to recognize in infancy, repeated episodes of hypernatremia may lead to mental retardation. In later years, the development of megaureter and bladder may partially mask the polyuria and nocturia. Hypercalcemia and hypokalemia can both cause nephrogenic diabetes insipidus.

Forms of renal disease that affect medullary concentrating structures may be associated with vasopressin-resistant hyposthenuria. Medullary cystic disease, analgesic nephropathy, obstructive nephropathy, sickle cell disease, Sjögren's syndrome, and pyelonephritis are examples. Lastly, certain medications (e.g., lithium, amphotericin B, demethylchlortetracycline, and methoxyflurane) interfere with the renal action of vasopressin and can cause nephrogenic diabetes insipidus. The rare compulsive water drinker makes a persistently dilute urine and complains of polyuria and nocturia.

A solute diuresis may be caused by increased endogenous or exogenous solute loads. Uncontrolled diabetes mellitus with hyperglycemia and glycosuria is the classic endogenous solute diuresis. Increased urea excretion with polyuria occurs in hypercatabolic states. Total parenteral nutrition with hypertonic glucose and both essential and nonessential amino acids may cause polyuria and nocturia because of both glycosuria and increased urea excretion. Other agents that may produce a significant solute diuresis include saline, mannitol, and radiocontrast media.

Both increased solute excretion and vasopressin-resistant hyposthenuria (combined solute and water diuresis) occur in the recovery phase of severe renal injury. This results from the large quantities of retained urea and sodium, as well as refractoriness to vasopressin. This type of polyuria and nocturia characterizes the early period following relief of bilateral urinary obstruction, the recovery phase of acute tubular necrosis, and, often, the early postrenal transplantation period.

References

Hillier P, Knapp MS, Cove-Smith R. Circadian variations in urine excretion in chronic renal failure. J Med 1980;49:461–78.

Kirkland JL, Lye M, Levy DW, et al. Patterns of urine flow and electrolyte excretion in healthy elderly people. Br Med J 1983;287:1665–67.

*Schrier RW, de Torrente A. Polyuria and nocturia. In: Massry S, Glassock R, eds. Textbook of nephrology. Baltimore: Williams and Wilkins, 1983;4.6–4.11.

Wesson LG. Electrolyte excretion in relation to diurnal cycles of renal function. Medicine 1964;43:547–92.