Nocturia: “Do the Math”

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Purpose: We reviewed the definition and etiologies of nocturia, offering the current diagnostic procedures and standards of care.

Materials and Methods: We reviewed recent published literature regarding nocturia, along with current paradigms for diagnosis and management.

Results: Nocturia is common as a limited occurrence but troublesome if the patient regularly experiences more than 2 episodes during sleep hours. The 4 principle etiologies associated with nocturia (nocturnal polyuria, decreased nocturnal bladder capacity, mixed polyuria, and global polyuria) may be easily differentiated through mathematical analysis of a 24-hour bladder diary.

Conclusions: Nocturia is highly treatable in many patients. Identification of the precise type and its cause enable clinicians to minimize the inconvenience and sleep deprivation associated with nocturia.

Key Words: urination disorders, polyuria, bladder

The International Continence Society definition of nocturia is the condition of waking up to void 1 or more times during the night.¹ A stricter definition would be voiding that is preceded and followed by sleep. This is an important distinction, because more than 15 million of the general population are shift workers who sleep during the day.² Nocturia is not necessarily troublesome; voiding fewer than 2 times per night generally is considered normal.

There are numerous scientific questions related to this definition. For example, how should sleep time be defined? Sleep time varies by individual, but on average, it is 8 hours per night. This can affect the evaluation of nocturia, because the number of nocturnal voids depends partly on how many hours an individual actually sleeps. Another question concerns whether the patient is awakened by the need to void, or if the patient voids after being awakened for some other reason.

For the purposes of evaluating nocturia, there are 2 basic categories: those with medical causes originating outside of the lower urinary tract, and those with urological causes. The former generally will be related to nocturnal urine overproduction (defined as nocturnal polyuria) or global polyuria. They can often be treated by a PCP or internist. The latter includes conditions requiring treatment by a urologist; these conditions generally are associated with decreased nocturnal bladder capacity.

DIFFERENTIAL DIAGNOSIS AND TREATMENT

Four general categories distinguishing causes of nocturia have been identified: 1) nocturnal polyuria, or nocturnal urine overproduction, 2) decreased nocturnal bladder capacity (low NBC), 3) mixed, which is a combination of the previous 2, and 4) global polyuria, that is urine overproduction throughout a 24-hour period. Appendix 1 lists the common causes of nocturia. A bladder diary and calculator are the key tools for generating a differential diagnosis of nocturia. “Doing the math” will elucidate the etiology of nocturia in most cases.

Ni is calculated by dividing NUV by MVV, previously referred to as functional bladder capacity.³ If Ni is greater than 1, nocturia occurs because MVV is exceeded by NUV (Appendix 2). It is important to note that the first morning void is not considered a nocturnal void, although the urine volume from that void is counted toward the NUV.

Nocturnal polyuria. Nocturnal polyuria refers to overproduction of urine during sleep hours. The formula for calculating NPi is simply NUV divided by 24-hour urine volume (Appendix 2). If 24-hour urine production is within normal limits, NPi greater than 35% is indicative of nocturnal polyuria.⁴ NPi increases with age, but even in the elderly population, NUV should be less than 34%. NPi has been variously defined as NUV greater than 6.4 ml/kg per sleep cycle, or nocturnal diuresis greater than 0.9 ml per minute (approximately 450 ml per 8 hours).

Nocturnal polyuria may be secondary to congestive heart failure; diabetes mellitus; obstructive sleep apnea; peripheral edema due to venous stasis or lymphostasis, nephrotic syndrome, hepatic failure, or hypoalbuminemia; or life-style patterns such as excessive nighttime drinking. Sleep apnea, which is defined as a sudden cessation of respiration due to airway obstruction during sleep,⁵ is an important factor in this equation. The mechanism is not an increase in trans-thoracic pressure by airway occlusion, as might be expected; it is increased airway resistance, subsequent hypoxemia, and pulmonary vasoconstriction. The latter causes a right atrial pressure increase, followed by diuresis mediated by atrial natriuretic peptide. Sleep apnea is often overlooked as...
of sleep. Decreased NBC can be related to decreased
capacity is defined as the largest voided volume during the
is secondary to a urological disorder. Nocturnal bladder ca-
tion is required in cases of decreased NBC, since this usually
or internist. It generally is held that a urological consulta-
tion with a urologist. Antimuscarinics and antispasmodic
agents may be prescribed as symptomatic treatment for
requirement in patients with decreased NBC. In determining man-
agement in patients with mixed etiology nocturia, it is recom-
nocturnal polyuria and decreased NBC. In determining man-
agement of these disorders is discussed more fully in
other articles in this journal supplement.

Mixed nocturia. A significant number of nocturia cases
are related to more than 1 etiology. “Mixed” nocturia is a
combination of nocturnal polyuria and decreased NBC, and
it is more common than many realize. In a study of 194
patients in whom nocturia was a chief or significant com-
plaint, 7% were determined to have simple nocturnal poly-
uria, 57% had decreased NBC, and 36% had a mixed
etiology, combining the first 2 etiologies.3 (The remaining
23% of patients had global polyuria, which will be discussed
later in this article.) Thus, nocturnal polyuria was a factor in
nocturia in 43% of the patients evaluated. It was concluded
that the etiology of nocturia was multifactorial and often
unrelated to an underlying urological condition, such as
prostatism.

Mixed nocturia is diagnosed through the maintenance and
analysis of bladder diaries. Through the formulas noted in
Appendix 2, it is possible to assess the relative contribution
of nocturnal polyuria and decreased NBC. In determining man-
agement in patients with mixed etiology nocturia, it is recom-
med that the simplest, least invasive, lowest risk treatment
should be attempted first. For example, elderly patients with
peripheral edema and nocturnal polyuria would be advised to
take an afternoon nap and wear compressive stockings. If there
is a compelling reason to recommend invasive treatment, such
as with bladder cancer or severe prostatic obstruction, that
should be addressed immediately.

As another example of “doing the math,” in a patient with
an NBCi of 3 and an NPi of 25%, it would be appropriate to
identify the cause of nocturnal detrusor overactivity and
 treat that first. This is a urological issue requiring consul-
tation with a urologist. Antimuscarinics and antispasmodic
agents may be prescribed as symptomatic treatment for
overactive bladder.

Global polyuria. The fourth category of nocturia etiology
is global polyuria, which is continuous overproduction of
urine not limited to sleep hours. Global polyuria is defined as
24-hour urine output of more than 40 ml/kg. (In a person
weighing 70 kg, this would be approximately 2,800 ml.) The
result is both diurnal and nocturnal overproduction of urine.
The common causes of global polyuria are diabetes mellitus,
DI, and primary thirst disorders.

The less common form of diabetes, DI, is a disorder of
water balance in the body. Inappropriate excretion of urine
may lead to polydipsia to prevent circulatory collapse. Central DI is caused by deficient synthesis of antidiuretic hormone secondary to the loss of neurosecretory neurons in the hypothalamus or posterior hypophysis. In nephrogenic DI, the pituitary gland produces a normal amount of antidiuretic hormone, but the kidneys do not respond appropriately to it. Diagnosis is made by overnight water deprivation test. (Note that if polyuria is suspected, overnight water deprivation carries certain risks and should be done in a clinical research unit.) If the first morning void is not highly concentrated, DI is diagnosed. Central DI usually can be treated with desmopressin. Nephrogenic DI may be treated with judicious regulation of fluid intake.

If the water deprivation test is normal in a patient experiencing polyuria, the diagnosis is a primary thirst disorder such as polydipsia, which may be either dipsogenic or psychogenic. In polydipsia, the patient demonstrates normal renal concentrating capacity. Dipsogenic polydipsia, which is very uncommon, is associated with a history of brain trauma or radiation that causes central nervous system dysfunction. This is generally easy to determine through medical history. Unfortunately, there is no recognized treatment for this form of polydipsia. Psychogenic polydipsia is the more common form; it is a long-term behavioral or psychological disorder involving compulsive fluid intake, which leads to polyuria. Treatment involves behavioral modification to decrease fluid intake; patients are often resistant to making such changes.

**CONCLUSIONS**

Nocturia is not necessarily troublesome, but patients experiencing more than 2 episodes per night often desire relief. Bladder diaries and formulas for the various indexes related to nocturia can determine which of 4 etiologies is present. Treatment should be tailored to the condition causing nocturia. Treatment of medical etiologies generally can be handled by a PCP or internist; referral to a urologist is recommended in cases involving urological etiologies, particularly those involving decreased NBC.

**APPENDIX 1**

<table>
<thead>
<tr>
<th>Classification of nocturia</th>
<th>Category</th>
<th>Causes</th>
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<tbody>
<tr>
<td>Nocturnal polyuria</td>
<td>Congestive heart failure</td>
<td>Diabetes mellitus</td>
</tr>
<tr>
<td></td>
<td>Obstructive sleep apnea</td>
<td>Peripheral edema</td>
</tr>
<tr>
<td></td>
<td>Excessive nighttime fluid intake</td>
<td>Prostatic obstruction</td>
</tr>
<tr>
<td></td>
<td>Nocturnal detrusor overactivity</td>
<td>Neurogenic bladder</td>
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<tr>
<td></td>
<td></td>
<td>Cancer of bladder, prostate, or urethra</td>
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<tr>
<td></td>
<td></td>
<td>Learned voiding dysfunction</td>
</tr>
<tr>
<td></td>
<td>Anxiety disorders</td>
<td>Pharmacological agents</td>
</tr>
<tr>
<td></td>
<td>Bladder calculi</td>
<td>Ureteral calculi</td>
</tr>
<tr>
<td></td>
<td>Diabetes mellitus</td>
<td>Diabetes insipidus</td>
</tr>
<tr>
<td></td>
<td>Primary polydipsia</td>
<td>*</td>
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</table>

**APPENDIX 2**

### Formulas for nocturia evaluation

<table>
<thead>
<tr>
<th>Formula</th>
<th>Analysis</th>
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<tbody>
<tr>
<td>Nocturia index</td>
<td>Ni = NUV - MVV</td>
</tr>
<tr>
<td>Nocturnal polyuria index</td>
<td>Ni &gt;1 → nocturia is due to NUV exceeding MVV</td>
</tr>
<tr>
<td>Nocturnal bladder capacity index</td>
<td>Ni - 1 = PNV*</td>
</tr>
<tr>
<td>NBCi - ANV - PNV</td>
<td>NBCi &gt;0 → nocturia occurring at volumes &lt; MVV</td>
</tr>
</tbody>
</table>

* Round up to next higher number if Ni - 1 is not an integer

### Abbreviations and Acronyms

- ANV = actual number of nightly voids
- AVP = arginine vasopressin
- DI = diabetes insipidus
- MVV = maximum voided volume
- NBC = nocturnal bladder capacity
- NBCi = NBC index
- Ni = nocturia index
- NPi = nocturnal polyuria index
- NUV = nocturnal urine volume
- PCP = primary care physician
- PNV = predicted number of nightly voids

### REFERENCES