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## CLINICAL VIGNETTE

# Nocturia: A Common Problem in The Elderly: A Clinical Vignette

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### *Case Report*

A 77-year-old male with a history of coronary artery disease, hypertension, spinal stenosis, and BPH presents with a long history of nocturia. The patient has seen multiple urologists in the past and has been prescribed various medications with little to no change in his nighttime symptoms. His symptoms include disabling nocturia that awakens him approximately every 45-60 minutes throughout most nights and has led to significant sleep deprivation. He avoids alcohol intake and restricts his caffeine intake to the early morning hours but symptoms have persisted. He has no fevers, dysuria, dyspnea, or other symptoms at this time.

Past medical history includes CAD s/p stent with PTCA, hyperlipidemia, hypertension, BPH, left knee replacement (2010), and spinal stenosis. Social history is unremarkable. He is a non-smoker who rarely drinks alcohol. He has at most one cup of coffee each morning. Medications include atorvastatin 40 mg daily, aspirin 81 mg daily, clopidogrel 75 mg daily, nifedipine XL 30 mg daily, Atenolol 50 mg twice daily, valsartan 160 mg two daily, oxaprozin 600 mg one daily prn, a laxative.

Physical examination reveals BMI is 31.2, blood pressure 140/80 without orthostatic change, pulse 64 and regular, and temperature 98.0 F. Physical exam is otherwise unremarkable with a normal cardiac and pulmonary exam with no edema.

Laboratory evaluation revealed a normal CBC but his chemistries revealed a creatinine of 1.6 mg/dL (stable over the past ten years). Otherwise, his basic blood work and urinalysis were unremarkable.

### *Discussion*

Nocturia (defined as waking at night to void) is a very common complaint especially in the elderly and is a common problem faced by primary care physician<sup>1</sup>. Nocturia is highly related to quality of life measures, psychiatric symptoms, sleep disorders, and is even associated with an increased all-cause mortality rate<sup>2,3</sup>. Of note, nocturia is commonly associated with falls and resultant injuries in the

elderly and can play a part in significant morbidity in this population<sup>4,5,6</sup>. Despite the seriousness of this problem, nocturia often presents a challenging diagnostic and treatment dilemma for the clinician<sup>7</sup>.

### *Epidemiology*

Nocturia is a very common disorder, which is reported in approximately 50% of patients over 50 years<sup>8</sup>. Before the age of 50, nocturia is more common in women than men but this distribution is reversed after the age of 60 years when nocturia becomes more common in men<sup>9</sup>. Although nocturia is defined as any nighttime awakening to void, clinically significant complications are usually only present in the patients who void two or more times each night<sup>10</sup>. There are many risk factors for nocturia including hypertension, snoring, BPH, coronary artery disease, CHF, diabetes, and obesity<sup>11</sup>. Nocturia is also a very common complaint during and after pregnancy<sup>12</sup>.

### *Clinical Features*

Nocturia does not usually present acutely but rather with a slow, gradual onset worsening over months or years<sup>13</sup>. Thus, it is very important for the clinician to specifically ask about nocturia as patients will commonly not mention it during office visits<sup>14</sup>. In addition, nocturia often displays a significant variation in severity from night to night make it a very frustrating problem for patients and clinicians<sup>15</sup>. This variation can play a large part in the disabling nature of the problem<sup>16</sup>. Daytime fatigue, nighttime frustration, and contributing medical problems such as CAD, CHF, diabetes, and BPH should also be considered as a part of the clinical picture in many of these patients<sup>17</sup>. A careful history of medication and supplement use should be obtained from patients. A nutritional intake history should also be obtained. Medications and supplements, as well as some dietary habits (especially alcohol, caffeine, and salt intake), can be common contributing factors to nocturia<sup>18</sup>.

### *Etiology and Pathophysiology*

There are many causes of nocturia with the most common being increased nighttime urinary output, low bladder volumes, bladder outlet obstruction, sleep disorders, and depression<sup>19</sup>. In general, younger patients tend to have lower bladder capacity as a contributing factor while older patients are more likely to have increased nighttime urination, bladder outlet obstruction, or sleep disorders as contributing factors<sup>20</sup>. Most patients have two or more factors contributing to the nocturia symptoms<sup>21</sup>.

The most common cause of nocturia tends to be small volume bladder voids which can result from limited bladder capacity, bladder outlet obstruction, or an oversensitive bladder. These issues increase with age mainly because of the increased prevalence of detrusor hyperactivity and BPH with age<sup>22</sup>. The other major cause of nocturia is increased nighttime urinary volume which can be caused by increased total urinary output or because of greater nighttime urinary volumes<sup>22</sup>. Increased total urinary output (polyuria) can be caused by certain medications (diuretics), poorly controlled diabetes, primary polydipsia, or due to an overconsumption of fluids. Increased nighttime urinary volumes can be caused by age-related changes in the production of arginine vasopressin<sup>18</sup>. Other causes of increased nighttime urination include solute diuresis (primarily due to ingesting food and beverages late at night), edematous states (such as CHF and nephrotic syndrome), and autonomic dysfunction syndromes (such as Parkinson's disease)<sup>23</sup>. Interestingly, the supine sleep position allows for increased mobilization of solutes and fluids from the third space into the blood stream, which can contribute to nocturia.

Nocturia can also be related to or caused by various sleep disorders<sup>24</sup>. About 50% of patients with sleep apnea complain of nocturia<sup>25</sup>. Some have postulated that the symptoms of nocturia be used to screen for sleep disorders<sup>26</sup>. In general, it is believed that nocturia can both be a symptom of sleep disorders or a contributing factor in causing sleep disorders<sup>27</sup>. Hormonal changes related to sleep disorders may possibly contribute to nocturia<sup>28</sup>. Also, patients may not accurately identify the cause of nighttime awakening as related to a sleep disorder. Some studies found up to 75% of all episodes of nocturia were triggered by apnea, snoring, or leg movements<sup>29</sup>. Sleep apneic episodes can trigger the release of atrial natriuretic peptide resulting in a cascade of chemical reactions leading to increased sodium and water excretion<sup>30</sup>. These effects are significantly reduced when the apnea is treated with various measures such as CPAP<sup>31</sup>. Nocturia may also

be related to depressive symptoms but it's not known if this association is related to the disease process or the medications used to treat it<sup>32</sup>.

### ***Diagnosis and Testing***

As with most disorders, history is paramount to properly diagnose and treat nocturia. Most clinicians start by asking patients how many times they wake up at night to void, as well as how disruptive the symptoms have been. If the history confirms a suspicion for nocturia then a full history of medication usage, other urinary symptoms, and medical conditions should be obtained. The history should focus on the quantity and timing of fluid intake, the intake of caffeine, the intake of alcoholic beverages, and the intake of prescription and over-the-counter medications.

A thorough physical examination should be performed with careful attention to the cardiovascular exam, abdomen exam, and orthostatic vital signs.

Preliminary testing often includes a 24-hour patient recording of void times and void amounts. By definition, nighttime urination includes urine produced after bedtime so this calculation does not include urination immediately before bedtime but does include urination on awakening. Typically, the patient is considered to have nocturia if the nocturnal urinary output is greater than 35% of total urinary output. Other tests that are often checked in patients with nocturia include the post-void residual, peak urinary flow rate, electrolytes, serum glucose, and creatinine. A urinalysis is usually checked and a urine culture if infection is suspected.

### ***Treatment***

The treatment of nocturia is very challenging and suboptimal results are the norm. A slight decrease in the frequency of episodes or the impact of episodes is typically the goal of therapy<sup>13</sup>. The initial treatment usually involves adjustments of the quantity and timing of fluid intake. A reduction in caffeine and alcohol consumption is usually recommended. Treating medical conditions such as diabetes, CHF, and dependent edema is also important. Other treatments are broadly classified as pharmacologic, behavioral, and experimental.

#### **1. Pharmacologic**

Pharmacologic options are many although none are highly effective. Alpha-1-adrenergic antagonists can sometimes be helpful in modestly controlling BPH

symptoms such as nocturia<sup>33</sup>. Reductions in nocturia are mild at best and tend to occur within weeks of starting the medication<sup>34</sup>. Side effects with these medications are common and include dizziness and orthostasis<sup>35</sup>. 5-alpha reductase inhibitors are also sometimes prescribed and can take up to 4-6 months to become fully effective. Although some studies have shown that 5-alpha reductase inhibitors can help with nocturia, the benefits have tended to be very slight<sup>36</sup>. Bladder relaxant medications such as oxybutynin, tolterodine, and solifenacin are sometimes prescribed and can be beneficial for some patients<sup>37</sup>. Their role is limited by side effects such as dry mouth which can be bothersome<sup>38</sup>. Antidiuretic therapies such as desmopressin is commonly used in Europe although it has not been approved for nocturia in the United States<sup>39</sup>. Patient on desmopressin need to be carefully monitored for hyponatremia especially in older patients with cardiac disease<sup>40</sup>.

## 2. Behavioral

Behavioral therapy emphasizing pelvic muscle training exercises can sometimes be useful for women with urge incontinence with nocturia<sup>41</sup>. Men can also benefit from pelvic floor muscle exercises in conjunction with pharmacologic measures<sup>39</sup>.

## 3. Newer Therapeutic Options

There are several novel therapies being tried for nocturia. Posterior tibial nerve stimulation where a transcutaneous needle is placed near the ankle has been tried with some positive results<sup>42</sup>. An implantable sacral nerve stimulator (interstim) is also sometimes tried and appears to be helpful for some patients<sup>43</sup>. Sleep medications such as melatonin have been tried for nocturia and the benefit appears to be in mitigating the bother of symptoms rather than a significant reduction in actual symptoms<sup>44</sup>. As medications have been found to have limited effectiveness, the use of combination therapy has become more widespread.<sup>45</sup>

### *Clinical Course and Follow-Up*

The patient tried numerous medications without much success. He also adjusted his lifestyle as much as possible including cutting back on caffeine and alcohol. The nocturia became more significant over time disrupting his sleep and leading to severe daytime fatigue. Eventually, he had a sacral nerve stimulator placed by his urologist, which helped considerably.

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