

## CLINICAL VIGNETTE

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

By Brian S. Morris, MD

### *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.

## REFERENCES

1. **Van Dijk MM, Wijkstra H, Debruyne FM, De La Rosette JJ, Michel MC.** The role of nocturia in the quality of life of men with lower urinary tract symptoms. *BJU Int.* 2010 Apr;105(8):1141-6. PubMed PMID: 22299137.
2. **Kupelian V, Fitzgerald MP, Kaplan SA, Norgaard JP, Chiu GR, Rosen RC.** Association of nocturia and mortality: results from the Third National Health and Nutrition Examination Survey. *J Urol.* 2011 Feb;185(2):571-7. doi: 10.1016/j.juro.2010.09.108. Epub 2010 Dec 18. PubMed PMID: 21168875.
3. **Middelkoop HA, Smilde-van den Doel DA, Neven AK, Kamphuisen HA, Springer CP.** Subjective sleep characteristics of 1,485 males and females aged 50-93: effects of sex and age, and factors related to self-evaluated quality of sleep. *J Gerontol A Biol Sci Med Sci.* 1996 May;51(3):M108-15. PubMed PMID: 8630703.
4. **Vaughan CP, Brown CJ, Goode PS, Burgio KL, Allman RM, Johnson TM 2nd.** The association of nocturia with incident falls in an elderly community-dwelling cohort. *Int J Clin Pract.* 2010 Apr;64(5):577-83. doi:10.1111/j.1742-1241.2009.02326.x. PubMed PMID: 20456212; PubMed Central PMCID:PMC3222329.
5. **Stewart RB, Moore MT, May FE, Marks RG, Hale WE.** Nocturia: a risk factor for falls in the elderly. *J Am Geriatr Soc.* 1992 Dec;40(12):1217-20. PubMed PMID:1447437.
6. **Temml C, Ponholzer A, Gutjahr G, Berger I, Marszalek M, Madersbacher S.** Nocturia is an age-independent risk factor for hip-fractures in men. *Neurourol Urodyn.* 2009;28(8):949-52. doi: 10.1002/nau.20712. PubMed PMID: 19301408
7. **Weiss JP, Blaivas JG.** Nocturia. *Curr Urol Rep.* 2003 Oct;4(5):362-6. Review. PubMed PMID: 14499058.
8. **Fitzgerald MP, Litman HJ, Link CL, McKinlay JB; BACH Survey Investigators.** The association of nocturia with cardiac disease, diabetes, body mass index, age and diuretic use: results from the BACH survey. *J Urol.* 2007 Apr;177(4):1385-9. PubMed PMID: 17382738.
9. **Tikkinen KA, Tammela TL, Huhtala H, Auvinen A.** Is nocturia equally common among men and women? A population based study in Finland. *J Urol.* 2006 Feb;175(2):596-600. PubMed PMID: 16407003.
10. **Tikkinen KA, Johnson TM 2nd, Tammela TL, Sintonen H, Haukka J, Huhtala H, Auvinen A.** Nocturia frequency, bother, and quality of life: how often is too often? A population-based study in Finland. *Eur Urol.* 2010 Mar;57(3):488-96. doi: 10.1016/j.eururo.2009.03.080. Epub 2009 Apr 3. PubMed PMID: 19361907.
11. **Johnson TM 2nd, Sattin RW, Parmelee P, Fultz NH, Ouslander JG.** Evaluating potentially modifiable risk factors for prevalent and incident nocturia in older adults. *J Am Geriatr Soc.* 2005 Jun;53(6):1011-6. PubMed PMID: 15935026.
12. **Viktrup L.** The risk of lower urinary tract symptoms five years after the first delivery. *Neurourol Urodyn.* 2002;21(1):2-29. PubMed PMID: 11835420.
13. **Weiss JP, Wein AJ, van Kerrebroeck P, Dmochowski R, Fitzgerald M, Tikkinen KA, Abrams P.** Nocturia: new directions. *Neurourol Urodyn.* 2011 Jun;30(5):700-3. doi: 10.1002/nau.21125. Review. PubMed PMID: 21661016.
14. **Michel MC, Oelke M, Goepel M, Beck E, Burkart M.** Relationships among symptoms, bother, and treatment satisfaction in overactive bladder patients. *Neurourol Urodyn.* 2007;26(2):190-5. PubMed PMID: 17096320.
15. **Häkkinen JT, Hakama M, Shiri R, Auvinen A, Tammela TL, Koskimäki J.** Incidence of nocturia in 50 to

- 80-year-old Finnish men. *J Urol.* 2006 Dec;176(6 Pt 1):2541-5; discussion 2545. PubMed PMID: 17085153.
16. **Booth J, McMillan L.** The impact of nocturia on older people – implications for nursing practice. *Br J Nurs.* 2009 May 28;18(10):592-6. PubMed PMID: 19491732.
  17. **Chang SC, Lin AT, Chen KK, Chang LS.** Multifactorial nature of male nocturia. *Urology.* 2006 Mar;67(3):541-4. PubMed PMID: 16527575.
  18. **Weiss JP, Blaivas JG, Stember DS, Chaikin DC.** Evaluation of the etiology of nocturia in men: the nocturia and nocturnal bladder capacity indices. *Neurourol Urodyn.* 1999;18(6):559-65. PubMed PMID: 10529704.
  19. **Weiss JP, Blaivas JG.** Nocturia. *J Urol.* 2000 Jan;163(1):5-12. Review. PubMed PMID: 10604303.
  20. **Weiss JP, Blaivas JG, Jones M, Wang JT, Guan Z;** 037 Study Group. Age related pathogenesis of nocturia in patients with overactive bladder. *J Urol.* 2007 Aug;178(2):548-51; discussion 551. Epub 2007 Jun 14. PubMed PMID: 17570424.
  21. **Vaughan CP, Endeshaw Y, Nagamia Z, Ouslander JG, Johnson TM.** A multicomponent behavioural and drug intervention for nocturia in elderly men: rationale and pilot results. *BJU Int.* 2009 Jul;104(1):69-74. doi: 10.1111/j.1464-410X.2009.08353.x. Epub 2009 Feb 11. PubMed PMID: 19220247.
  22. **Pfisterer MH, Griffiths DJ, Schaefer W, Resnick NM.** The effect of age on lower urinary tract function: a study in women. *J Am Geriatr Soc.* 2006 Mar;54(3):405-12. PubMed PMID: 16551306.
  23. **Kirkland JL, Lye M, Levy DW, Banerjee AK.** Patterns of urine flow and electrolyte excretion in healthy elderly people. *Br Med J (Clin Res Ed).* 1983 Dec 3;287(6406):1665-7. PubMed PMID: 6416541; PubMed Central PMCID: PMC1550090.
  24. **Hajduk IA, Strollo PJ Jr, Jasani RR, Atwood CW Jr, Houck PR, Sanders MH.** Prevalence and predictors of nocturia in obstructive sleep apnea-hypopnea syndrome—a retrospective study. *Sleep.* 2003 Feb 1;26(1):61-4. PubMed PMID: 12627734.
  25. **Moriyama Y, Miwa K, Tanaka H, Fujihira S, Nishino Y, Deguchi T.** Nocturia in men less than 50 years of age may be associated with obstructive sleep apnea syndrome. *Urology.* 2008 Jun;71(6):1096-8. doi: 10.1016/j.urology.2008.02.038. Epub 2008 Apr 8. PubMed PMID: 18400277.
  26. **Romero E, Krakow B, Haynes P, Ulibarri V.** Nocturia and snoring: predictive symptoms for obstructive sleep apnea. *Sleep Breath.* 2010 Dec;14(4):337-43. doi: 10.1007/s11325-009-0310-2. Epub 2009 Oct 29. PubMed PMID: 19865841.
  27. **Lowenstein L, Kenton K, Brubaker L, Pillar G, Undevia N, Mueller ER, FitzGerald MP.** The relationship between obstructive sleep apnea, nocturia, and daytime overactive bladder syndrome in women. *Am J Obstet Gynecol.* 2008 May;198(5):598.e1-5. doi: 10.1016/j.ajog.2008.02.024. PubMed PMID: 18455544.
  28. **Endeshaw YW, Johnson TM, Kutner MH, Ouslander JG, Bliwise DL.** Sleep-disordered breathing and nocturia in older adults. *J Am Geriatr Soc.* 2004 Jun;52(6):957-60. PubMed PMID: 15161461.
  29. **Pressman MR, Figueroa WG, Kendrick-Mohamed J, Greenspon LW, Peterson DD.** Nocturia. A rarely recognized symptom of sleep apnea and other occult sleep disorders. *Arch Intern Med.* 1996 Mar 11;156(5):545-50. PubMed PMID: 8604961.
  30. **Umlauf MG, Chasens ER, Greevy RA, Arnold J, Burgio KL, Pillion DJ.** Obstructive sleep apnea, nocturia and polyuria in older adults. *Sleep.* 2004 Feb 1;27(1):139-44. PubMed PMID: 14998251.
  31. **Krieger J, Laks L, Wilcox I, Grunstein RR, Costas LJ, McDougall JG, Sullivan CE.** Atrial natriuretic peptide release during sleep in patients with obstructive sleep apnoea before and during treatment with nasal continuous positive airway pressure. *Clin Sci (Lond).* 1989 Oct;77(4):407-11. PubMed PMID: 2530023.
  32. **Kupelian V, Wei JT, O'Leary MP, Norgaard JP, Rosen RC, McKinlay JB.** Nocturia and quality of life: results from the Boston area community health survey. *Eur Urol.* 2012 Jan;61(1):78-84. doi: 10.1016/j.eururo.2011.05.065. Epub 2011 Sep 10. PubMed PMID: 21945718; PubMed Central PMCID: PMC3226859.
  33. **Johnson TM 2nd, Jones K, Williford WO, Kutner MH, Issa MM, Lepor H.** Changes in nocturia from medical treatment of benign prostatic hyperplasia: secondary analysis of the Department of Veterans Affairs Cooperative Study Trial. *J Urol.* 2003 Jul;170(1):145-8. PubMed PMID: 12796667.
  34. **Lepor H, Williford WO, Barry MJ, Brawer MK, Dixon CM, Gormley G, Haakenson C, Machi M, Narayan P, Padley RJ.** The efficacy of terazosin, finasteride, or both in benign prostatic hyperplasia. Veterans Affairs Cooperative Studies Benign Prostatic Hyperplasia Study Group. *N Engl J Med.* 1996 Aug 22;335(8):533-9. PubMed PMID: 8684407.
  35. **Roehrborn CG, Van Kerrebroeck P, Nordling J.** Safety and efficacy of alfuzosin 10 mg once-daily in the treatment of lower urinary tract symptoms and clinical benign prostatic hyperplasia: a pooled analysis of three double-blind, placebo-controlled studies. *BJU Int.* 2003 Aug;92(3):257-61. PubMed PMID: 12887479.
  36. **Johnson TM 2nd, Burrows PK, Kusek JW, Nyberg LM, Tenover JL, Lepor H, Roehrborn CG;** Medical Therapy of Prostatic Symptoms Research Group. The effect of doxazosin, finasteride and combination therapy on nocturia in men with benign prostatic hyperplasia. *J Urol.* 2007 Nov;178(5):2045-50; discussion 2050-1. Epub 2007 Sep 17. PubMed PMID: 17869295.
  37. **Burgio KL, Goode PS, Johnson TM, Hammontree L, Ouslander JG, Markland AD, Colli J, Vaughan CP, Redden DT.** Behavioral versus drug treatment for overactive bladder in men: the Male Overactive Bladder Treatment in Veterans (MOTIVE) Trial. *J Am Geriatr Soc.* 2011 Dec;59(12):2209-16. doi: 10.1111/j.1532-5415.2011.03724.x. Epub 2011 Nov 7. PubMed PMID: 22092152.
  38. **Wagg A, Wyndaele JJ, Sieber P.** Efficacy and tolerability of solifenacin in elderly subjects with overactive bladder syndrome: a pooled analysis. *Am J Geriatr Pharmacother.* 2006 Mar;4(1):14-24. PubMed PMID: 16730617.
  39. **Moon DG, Jin MH, Lee JG, Kim JJ, Kim MG, Cha DR.** Antidiuretic hormone in elderly male patients with severe nocturia: a circadian study. *BJU Int.* 2004 Sep;94(4):571-5. PubMed PMID: 15329115.
  40. **Rembratt A, Norgaard JP, Andersson KE.** Desmopressin in elderly patients with nocturia: short-term safety and effects on urine output, sleep and voiding patterns. *BJU Int.* 2003 May;91(7):642-6. PubMed PMID: 12699476.
  41. **Johnson TM 2nd, Burgio KL, Redden DT, Wright KC, Goode PS.** Effects of behavioral and drug therapy on nocturia in older incontinent women. *J Am Geriatr Soc.* 2005 May;53(5):846-50. PubMed PMID: 15877562.
  42. **Peters KM, Carrico DJ, Perez-Marrero RA, Khan AU, Wooldridge LS, Davis GL, Macdiarmid SA.** Randomized trial of percutaneous tibial nerve stimulation versus Sham efficacy in the treatment of overactive bladder syndrome: results from the SUMiT trial. *J Urol.* 2010 Apr;183(4):1438-43. doi: 10.1016/j.juro.2009.12.036. Epub 2010 Feb 20. PubMed PMID: 20171677.

43. **Marinkovic SP, Gillen LM, Stanton SL.** Managing nocturia. *BMJ.* 2004 May 1;328(7447):1063-6. Review. PubMed PMID: 15117794; PubMed Central PMCID: PMC403853.
44. **Drake MJ, Mills IW, Noble JG.** Melatonin pharmacotherapy for nocturia in men with benign prostatic enlargement. *J Urol.* 2004 Mar;171(3):1199-202. PubMed PMID:14767300.
45. **Burgio KL, Locher JL, Goode PS.** Combined behavioral and drug therapy for urge incontinence in older women. *J Am Geriatr Soc.* 2000 Apr;48(4):370-4. PubMed PMID: 10798461.

*Submitted on March 27, 2013*