The dilemma of nocturia

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Cite as: *Can Urol Assoc J* 2012;6(5):S138-40. http://dx.doi.org/10.5489/cuaj.12203

Abstract

Patients with nocturia are often referred to urologists, but the underlying cause most often lies outside the urinary tract. Nocturia should be considered a systemic disorder and investigated and treated as such. Comprehensive assessment of the symptoms, optimally including a frequency volume chart, can help to determine the potential underlying cause and help to direct the patient to the most suitable medical professional for further management.

Although patients with nocturia are often referred to urologists, the underlying problem causing the problem most often lies outside the lower urinary tract. As such, it is more helpful to think of nocturia as a systemic disorder, rather than merely a lower urinary tract symptom (LUTS),[1] and to select treatment based on a proper evaluation for contributory factors.

Assessment of nocturia

Assessment of nocturia should seek to categorize patients according to the presence or absence of sleep disturbance, bladder storage issues, polyuria, and psychological or behavioural influences (Fig. 1).[2] A frequency volume chart is an indispensable tool to help characterize each individual patient's problem.[3]

Management of nocturia

There has been a substantial body of research conducted using LUTS-specific pharmacotherapies for nocturia. Statistically significant symptom improvements from LUTS pharmacotherapy or surgery have been reported, but should be reviewed critically. The placebo-adjusted improvement in the number of voids with alpha-blockers, antimuscarinics, and 5-alpha reductase antagonists (alone or in combination) is in the range of 0.08 to 0.3 per night.[4-11] Surgical management (prostatectomy) has been shown to reduce symptoms, but again, is far from curative. One analysis of prostatectomy showed that the nocturia frequency decreased from 3.4 preoperatively to 2.6 postoperatively.[12] Nonetheless, it is doubtful whether this is clinically significant.

These minimal improvements with LUTS-specific treatments have helped to drive the recognition of nocturia as a systemic disorder, necessitating access to multimodal investigation and multidisciplinary expertise, and obligates a shift away from a bias that the lower urinary tract is the main driver of nocturia. Other potential causes need to be investigated and treated when identified.

Patients with endocrine dysfunction

Nocturnal polyuria is potentially due to renal tubular[13] or endocrine dysfunction and fluid shifts, leading to diuresis/natriuresis. Desmopressin is effective in some patients, and new data are emerging to guide safe dosing,[14] including recognition of potential gender differences in response. Decrease in nocturnal urine volume in nocturia patients have been shown to be larger for women at lower desmopressin doses, and decreases in sodium greater in women over 50 years old than in men.[15]

Patients with sleep disturbances

Sleep disturbance can result from sleep disorders, medical/neurological/psychiatric disease and other influences, which need to be factored in by any urologist responsible for treating nocturia. Patients suspected of having a sleep disorder (e.g., sleep apnea, nocturnal seizures, excessive daytime sleepiness) should be referred to a sleep specialist.

In terms of therapy for sleep disturbances, an improvement in sleep hygiene (e.g., optimal room temperature, noise reduction, etc.) may be helpful for many patients. As a reflection of intrinsic circadian rhythm, the normal reduction in urine output during sleep is seen in alteration of key water-handling proteins of the kidney.[16] Accordingly, the key circadian hormone, melatonin, was studied in 20 men with urodynamically confirmed bladder outflow obstruction and nocturia (three or more times per night).[17] This was a randomized, double-blind, placebo-controlled crossover study assessing the effect of 2 mg controlled release melatonin at night. As shown in Table 1, a significantly greater proportion of patients responded to melatonin than to placebo, but responders were still in the minority in the active treatment group.

Table 1. Melatonin for nocturia: Responder rates (by episodes reduced per night) in a randomized, placebo-controlled crossover study

Responder definition	Melatonin	Placebo	*P* value	Mean bother reduction
-0.5	6	1	0.04	1.0
-1.0	3	0	0.07	1.7
-2.0	1	0	0.31	2.0

Adapted from Drake et al. Melatonin pharmacotherapy for nocturia in men with benign prostatic enlargement. *J Urol* 2004;171:1199-202.

Short-acting hypnotics may be helpful for patients with sleep disturbances. Oxazepam has been associated with a reduction in nocturia (but not nocturnal urine production).[18]

Global polyuria

For patients with global polyuria (>40 mL/kg/24h), the best approach may be behavioural modification (e.g., advise drinking to thirst, reduce salt intake). However, fluid restriction is not appropriate if an underlying cause of fluid loss is present, e.g., diabetes insipidus.

Nocturnal polyuria

Nocturnal polyuria may occur secondary to any renal tubular dysfunction, third space fluid sequestration, obstructive sleep apnea, circadian impairment or as a side effect of drugs (e.g., steroids).[19]

For those patients with suspected fluid sequestration (which is a possibility in patients with venous insufficiency, hypoalbuminemia, congestive cardiac failure, etc.), one can consider compression and elevation, or the use of a diuretic in the afternoon.[20,21]

Conclusions

The lower urinary tract is not the major cause of nocturia. One needs to assess the patient for underlying causes, recognizing that sleep disorders, polyuria and endocrine disease are the most likely causes. The management of nocturia may require a team approach, whenever possible, making optimal use of multidisciplinary expertise.

There is a need for better nocturia treatment algorithms based on screening measures and outcome prediction. Ultimately, these algorithms would incorporate simple screening measures to guide interdisciplinary referral and lead to the multidisciplinary teamwork that is required for full investigation and treatment success. This process should also help prevent the use of treatments for which symptomatic response cannot be anticipated.[19]

Competing interests: Prof. Drake is an ongoing paid consultant with Ferring. He has also received speaker fees, educational grants and/or travel assistance from Ferring , Allergan, Pfizer and Astellas within the last two years.

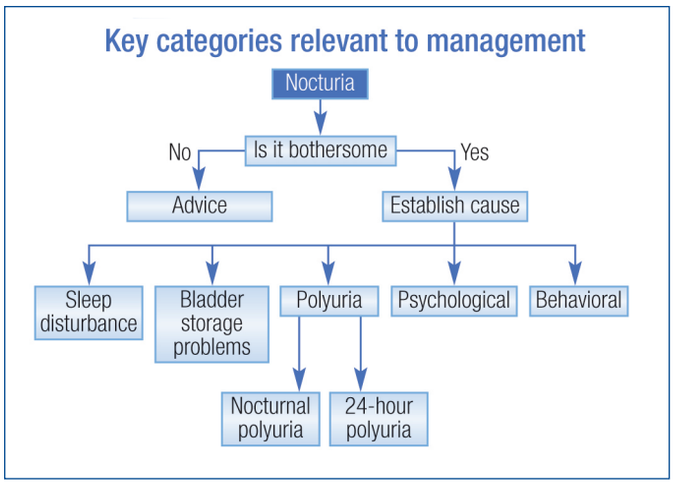

Fig. 1. Investigating potential causes of nocturia. Adapted from Wein et al. Nocturia in men, women and the elderly: a practical approach. *BJU Int* 2002;90(Suppl3):28-31.

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