Title:

Practical approach to diagnosis and management of nocturia

Authors:

J. Rees, M.Kirby, S. De Wachter, M. Drake, K. Everaert, A. Giannantoni, M. Oelke, S. Orme and P. van Kerrebroeck

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Introduction

Nocturia can have a profound impact on quality of life (QoL) and health outcomes, yet it continues to be underreported, undertreated and poorly managed. The term nocturia is defined by the International Continence Society (ICS) as 'the complaint that the individual has to wake at night one or more times to void... each void is preceded and followed by sleep.'[1,2] This definition is currently a topic of debate. A perhaps more practical and clinically relevant definition is two or more voids per night, as at this point it would become bothersome for most if not all individuals.[3–5] The definition for nocturnal polyuria has not been universally standardised, but is typically referred to as nocturnal urinary output that is greater than 20% of 24-hour urine volume in young adults, and 33% of 24-hour urine volume in older adults.[2] Nocturnal polyuria is the most frequent cause of nocturia, having been shown in studies to be partially or fully responsible for up to 88% of cases.[2,6,7] Patients may have multiple pathologies contributing towards their nocturia.[2,6,7] In this *Trends in Urology & Men's Health* supplement, the authors describe the epidemiology and medical conditions associated with nocturia, and provide primary care physicians with straightforward, practical recommendations and tools for its diagnosis and treatment, as well as advice on when specialist referral may be required.

Authors
Dr Jonathan Rees, GP with a special interest in urology, Nailsea, UK
Professor Mike Kirby, Professor, The Centre for Research in Primary and Community Care, The University of Hertfordshire and The Prostate Centre, London, UK
Professor Stefan De Wachter, Professor of Urology, University of Antwerp, Belgium
Professor Marcus Drake, Professor of Urology, University of Bristol, UK
Professor Karel Everaert, Professor in Neurourology, Ghent University Hospital, Belgium
Professor Antonella Giannantoni, Associate Professor of Urology, University of Perugia, Italy
Professor Matthias Oelke, Associate Professor for Urology, University of Maastricht, The Netherlands
Dr Susan Orme, Consultant in Geriatric Medicine, Barnsley Hospital NHS Foundation Trust Hospital, UK
Professor Philip van Kerrebroeck, Professor of Urology, University of Maastricht, The Netherlands

Corresponding author: Professor Mike Kirby, The Centre for Research in Primary and Community Care, The University of Hertfordshire and The Prostate Centre, London, UK

Declaration of interests
Jonathan Rees has been an advisor and speaker for Astellas, Ferring and Lilly. Mike Kirby has received funding for research, conference attendance, lecturing and advice from the pharmaceutical industry including Astellas, Pfizer, Takeda, Bayer, MSD, BI, Lilly, GlaxoSmithKline, AstraZeneca and Menarini. He is the Editor of PCCJ. He is also on several NHS advisory boards including the Prostate Cancer Risk Management Programme and the Prostate Cancer Advisory Group. Stefan De Wachter has been an advisor and speaker for Astellas, a speaker and advisor for and received a research grant from Medtronic, and an advisor to Allergan, Ferring, Lilly, Menarini and Pfizer. Marcus Drake has been an advisor, speaker and researcher with Allergan, Astellas and Ferring. Karel Everaert has received grants and honoraria as a speaker and advisor for Allergan, Astellas and Ferring. Antonella Giannantoni is a scientific consultant for Allergan, Astellas, Ferring and Menarini. Matthias Oelke has been a speaker, consultant and/or trial participant for Apogepha, Astellas, Bayer, GlaxoSmithKline, Ferring, Lilly and Pfizer. Susan Orme has been a speaker for Astellas, Ferring and Pfizer. Philip van Kerrebroeck has acted as advisor and speaker for Astellas, Ferring and Medtronic.

Practical approach to diagnosis and management of nocturia

AETIOLOGY AND BURDEN OF NOCTURIA

Recognising nocturia and determining its causes are crucial to treating it effectively. The vast majority of patients with nocturia/nocturnal polyuria will initially present to primary care. It is important, therefore, that primary care physicians are knowledgeable about the underlying causes, the patients at risk, the clinical causes, and the treatment options that are currently available. While traditionally regarded as a predominantly male condition, nocturia is very common in women.[8,9] The incidence in both sexes increases with age.[8,9]

Nocturia has traditionally been regarded as a symptom of benign prostatic hyperplasia (BPH) and/or overactive bladder (OAB) syndrome, with treatment therefore directed toward increasing the capacity of the bladder to hold urine. However, such treatments have proven largely ineffective in many patients because nocturnal polyuria, an overproduction of urine at night, has been found to be present in the majority of patients.[10] Nocturia should therefore be considered a distinct medical presentation in its own right, not necessarily driven by a lower urinary tract dysfunction involving the bladder, prostate, pelvic floor or urethra.[11]

There are several aetiological factors for nocturia, but the main pathophysiological mechanisms are related to the following issues:

1. Nocturnal polyuria
2. Global polyuria (daily urine volume greater than 40ml/kg; accordingly, urine volume in patients with global polyuria is greater than 2800ml/24 hours for a reference person with a body weight of 70kg)
3. Bladder storage disorders
4. Sleep impairment.

Awakening during deep sleep has a significant negative impact on sleep quality, and therefore on wellbeing and health.[3,5,12–15] This leads to tiredness and fatigue that can affect everyday activities and instrumental activities of daily living and, therefore, have a negative impact on QoL.[5,12] As nocturia causes the necessity to toilet at night, it is also an important cause of falls and fall-related fractures in the elderly population.[16–18]

Nocturia has also been shown to be a predictor of mortality, more so in

Box 1. Possible causative or contributing factors to the pathophysiology of nocturia[20–25]

NOCTURNAL POLYURIA
- Decrease in nocturnal urinary levels of arginine-vasopressin (AVP, naturally occurring anti-diuretic hormone)
- Increase in atrial natriuretic peptide
- Cardiac insufficiency, congestive heart failure
- Obstructive sleep apnoea
- Renal tubular dysfunction
- Hepatic failure
- Hypoalbuminaemia
- Diuretic usage (at evening)
- Lower extremity venous insufficiency
- Evening polydipsia
- Alcoholism

GLOBAL POLYURIA
- Diabetes mellitus
- Increasing water or liquid intake (habitual polydipsia)
- Renal insufficiency
- Diabetes insipidus
- Hypercalcaemia- and hypercalciuria-related diseases
- Oestrogen insufficiency in women

DECREASED (NOCTURNAL) BLADDER CAPACITY
- Overactive bladder
- Neurogenic detrusor overactivity
- Post-void residual urine due to bladder outlet obstruction, detrusor underactivity (*ie* detrusor contraction during voiding which is too weak or not long enough) or dysfunctional voiding
- Bladder hypersensitivity
- Urinary tract infection
- Bladder wall fibrosis
- Bladder tumour, stone, foreign body
- Interstitial cystitis
- Post-surgical bladder dysfunction

SLEEP DISTURBANCES
- Environmental impairments
- Anxiety disorders
- Depression
- Stimulant usage
- Melatonin deficiency of ageing

MEDICATIONS (EXACERBATING NOCTURIA OR POLYURIA)
- Calcium channel blockers (*eg* amlodipine)
- Thiazides
- GABA-ergic agents (*eg* gabapentin, pregabelin)

BEHAVIOURAL
- Habitual excessive fluid intake

relatively younger men and women than in the elderly.[19] Data from a survey undertaken in the USA demonstrated a significant trend for increased mortality risk with increasing number of nocturnal voiding episodes. Potential underlying mechanisms for this association included sleep disruption and the development of related comorbid conditions.[19]

The possible causative or contributing factors to the pathophysiology of nocturia, several of which may be present in the same individual, are shown in Box 1. A screening tool to aid identification and assessment of non-lower urinary tract comorbidities associated with nocturia has recently been published (TANGO: Targeting the individual's Aetiology of Nocturia to Guide Outcomes).[26]

CLINICAL PRESENTATION AND EVALUATION

Many patients with nocturia delay for a considerable time before seeking help or ultimately receiving treatment for their condition.[27,28] Recent evidence from a population of 8659 patients reported a mean time of 51 weeks from symptom (nocturia) onset to first consultation; 12 weeks from first consultation to diagnosis; and 37 weeks from diagnosis to first prescribed treatment.[28] Overall, the total (mean) time from symptom (nocturia) onset to treatment was 106 weeks.[28] In one survey of women aged ≥40 years reporting fewer than three nocturia episodes:[27]

Signs and symptoms	Presence/ absence	Diagnoses/further investigations to consider
Does the patient wake up in the night to pass urine?		Consider diagnosis of nocturnal polyuria
Would the patient rate nocturia as bothersome?		
Does the patient leak urine when they laugh, cough, sneeze, lift something heavy?		Symptoms suggestive of stress incontinence Consider a stress test
Does the patient have a sudden and urgent need to urinate, sometimes associated with urgency incontinence?		Symptoms suggestive of overactive bladder
Does the patient have the sensation that their bladder has not emptied fully?		Symptoms suggestive of bladder obstruction (*eg* bladder outlet obstruction, benign prostatic hyperplasia), bladder dysfunction, urinary tract infection Urinalysis to rule out urinary tract infection, consider testing renal function (eGFR) and renal/ bladder ultrasound
Does the patient have difficulty starting or maintaining a steady stream?		Suggestive of dysfunctional voiding, most commonly due to bladder outlet obstruction
Urinary frequency (≥8 voids/day)?		Consider a diagnosis of OAB – usually associated with urgency of micturition in addition to urgency
Female patients: Pre-menopause? Post-menopause? On hormone replacement therapy?		Consider oestrogen deficiency
Does the patient have any neck or back pain, or any limb weakness or sensory loss?		Assess neurological and spinal signs and symptoms (possible red flag – may require urgent referral)
Is the patient taking any medication that may precipitate nocturia? Calcium channel blockers (*eg* amlodipine) Thiazides GABA-ergic agents (*eg* gabapentin, pregabelin)		Give a trial without the medication to see if it is causing or exacerbating the condition, if appropriate Move diuretic doses to the mid-afternoon

Table 1. Checklist of various signs and symptoms, with diagnoses and possible further investigations to consider

Signs and symptoms	Presence/ absence	Diagnoses/further investigations to consider
Does the patient have any of the following medical conditions? Heart disease Hypertension Arthritis Diabetes mellitus Metabolic syndrome Asthma Irritable bowel syndrome Recurrent urinary tract infection Benign prostatic hyperplasia Prostatitis Prostate cancer Uterine prolapse Hysterectomy Menopausal status Anxiety and depression		Comorbidities that may be contributing to nocturia
Sleep history: Does the patient have a history of loud snoring or does breathing repeatedly stop and start during sleep (to be corroborated by partner)?		Suggestive of obstructive sleep apnoea – may be contributing to nocturia
Does the patient have a history of enuresis?		May be associated with chronic retention of urine – arrange bladder/renal ultrasound
Does the patient have any problems with sexual function?		Often associated with lower urinary tract symptoms
Is the patient overweight/obese?		
Drinking habits: Drinks more than one glass during the evening? Drinks during the night?		

Table 1. Checklist of various signs and symptoms, with diagnoses and possible further investigations to consider (continued)

- 66.4% thought nocturia was a minor problem
- 60.7% thought nocturia was part of the normal ageing process
- 31.3% did not see a doctor because they did not think nocturia was treatable
- 37.2% of women who had consulted a doctor were not offered any treatment.

It is important to enquire about nocturia as it is often underreported. Any elderly patient presenting with nocturnal falls should be asked about their voiding history. A thorough assessment of nocturia and its various causes should be undertaken before treatment initiation.[29] It is possible to determine the bother caused by nocturia if the correct questions are asked, which enables further investigation to determine the cause of the symptom. A checklist is provided to help primary care physicians assess the patient's signs and symptoms (Table 1). The checklist contains a number of questions to ask the patient and notes are given below to support a possible diagnosis.

Patient history, physical examination and laboratory tests give important clues to the underlying pathological processes (Box 2).

Given the wide range of possible aetiologies, the key diagnostic tool is the frequency-volume chart (FVC) (see page 11; see also the Dutch website www.opstaanomteplassen.be and Everaert *et al*[32]). FVCs objectively document the time of each void, voided volume per micturition, time of going to bed with the intention of sleeping, and the time of waking up with the intention of starting the

Box 2. Components of a basic assessment of patients with nocturia/nocturia due to nocturnal polyuria[30,31]

- Patient history
  - Fluid consumption, alcohol and caffeine consumption, urinary symptoms (including voiding and frequency), sleeping habits, medical history, symptoms of obstructive sleep apnoea (consider Epworth Sleepiness Scale or STOP-BANG[31])
- Review current medication to identify drugs that may be contributing to the problem
  - *eg* calcium channel blockers such as amlodipine, nifedipine
- Physical examination
  - Blood pressure, digital rectal examination of the prostate in men/pelvic examination in women, checking for oedema of the lower extremities, checking genitalia for any abnormalities, abdominal examination including palpation of the bladder to rule out urinary retention
  - Determine if patient is overweight/obese: measure weight/body mass index/waist circumference
- Investigations
  - Urinalysis (in all cases) with urine culture if urinary tract infection suspected, serum electrolytes and creatinine, serum glucose or HbA1c, lipids
- Prostate-specific antigen for prostate cancer (if clinically relevant) and estimation of prostate size

day.[29] Nocturnal urine volume describes the amount of urine excreted during the night time and also includes the volume of the first morning void after waking because this urine has been produced during the night time. Hence, it is important to include the first void of the morning in the total nocturnal urine volume when the chart is completed by the patient.

TREATMENT

Goals and expectations of treatment should be discussed with the patient. Based on the underlying causes, current treatment strategies include lifestyle modification and pharmacological therapies. A proposed evaluation and treatment algorithm for patients with nocturia/nocturia due to nocturnal polyuria is provided in Figure 1.

Lifestyle modification

Lifestyle modification should be the first intervention in the management of nocturia/nocturia due to nocturnal polyuria and should be discussed at every consultation (Box 3). Behavioural treatments and lifestyle interventions have not been the subject of thorough clinical investigations, but they are cheap and easy and, therefore, should be included in every treatment strategy.[29] Motivational interviewing techniques can be used to encourage and support appropriate lifestyle changes. While most patients are aware of the benefits of exercise and a healthy diet, every opportunity should be taken to move them from contemplation to action. Even in a short consultation, emphasising the importance of a healthy diet, physical activity and smoking cessation for reducing the risk of bladder cancer and the impact on lower urinary tract symptoms (LUTS) and nocturia, may encourage change. It should be recognised that the impact of lifestyle changes is slow – a three-month trial is a reasonable timescale unless bother is increasing. However, it is important that the duration of lifestyle/behavioural modification is individualised based on symptom severity, symptom bother, comorbidities and patient preference, etc.

Medical management

If behavioural treatments and lifestyle interventions fail, treatment with pharmacological agents is indicated. Treatment depends on the underlying cause. Pharmacological agents include diuretics, antidiuretic agents (desmopressin), antimuscarinic agents and alpha-adrenergic blockers. These medications have been reviewed by the International Consultation on Urological Diseases (ICUD) committee and the evidence for many of them was found to be weak.[33] Available data, however, support the use of desmopressin for patients with nocturia due to nocturnal polyuria.[34–37]

Diuretic therapy

The evidence supporting the efficacy of diuretics in treating nocturia is low. Appropriately timed diuretic therapy may be an effective treatment strategy for nocturia of unknown aetiology. In patients with nocturnal polyuria owing to reabsorption of third-space lower extremity fluid in the supine position during sleep, loop diuretics should be administered in the mid-afternoon to address fluid accumulated over the course of the day, but not so late as to actually exacerbate nocturnal polyuria.[38]

Antidiuretic therapy

Desmopressin, a selective vasopressin type 2 (V_2) receptor agonist, is the drug that has been the most frequently used for specific management of nocturia due to nocturnal polyuria.[25] Desmopressin is a synthetic analogue of the human hormone AVP, aiming at concentrating the urine at night by way of an action on V_2 receptors present in the distal collecting tubules.[25]

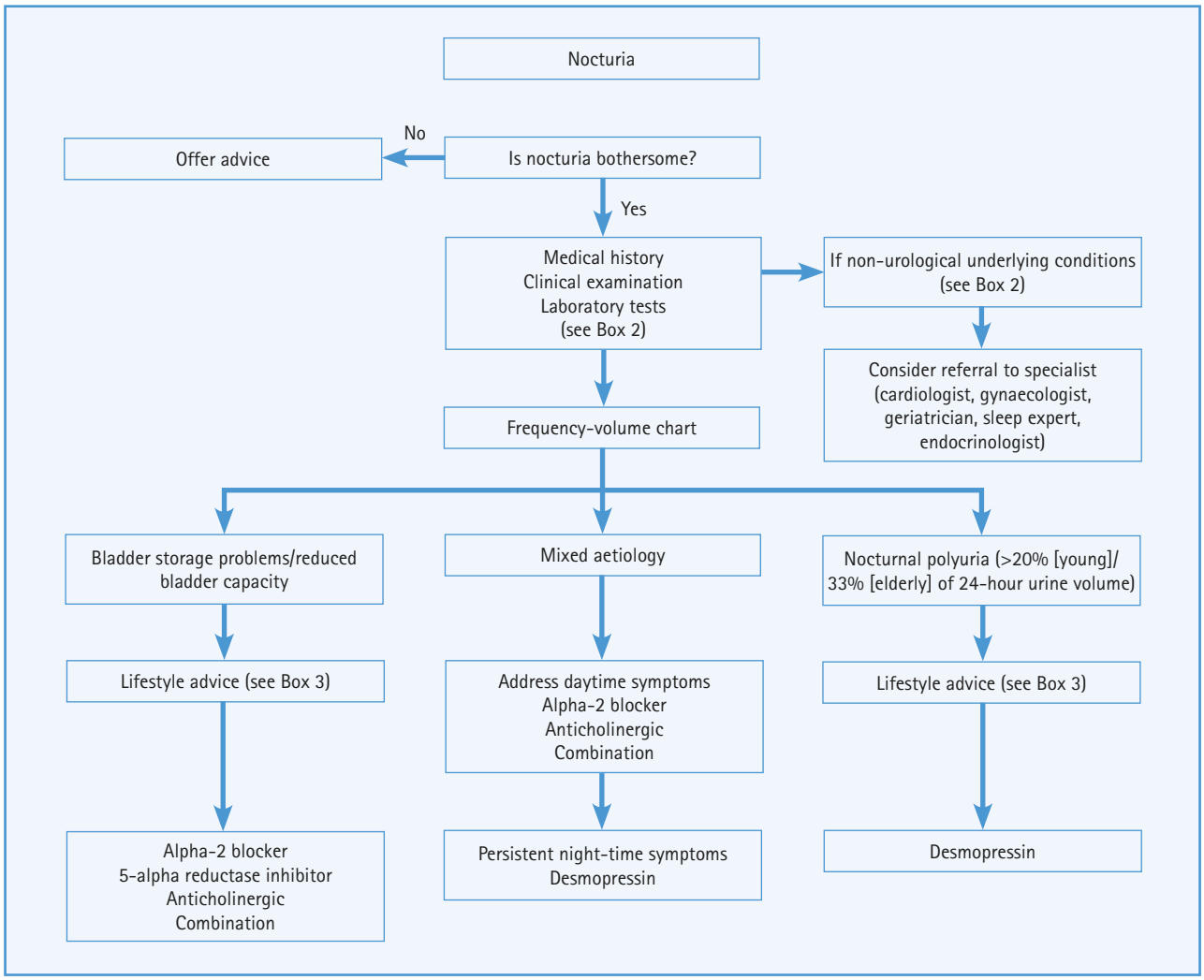

Figure 1. Evaluation and treatment algorithm for nocturia/nocturia due to nocturnal polyuria

Randomised placebo-controlled trials have shown that oral desmopressin is an effective and well tolerated treatment in male and female adults with nocturia due to nocturnal polyuria.[34–36] Studies into optimal dosing suggest a lower dose of desmopressin orally disintegrating tablet may be more effective in females than in males with nocturia.[34] A pooled analysis of three randomised, placebo-controlled trials demonstrated that the short-term benefits of desmopressin therapy are maintained and even enhanced over the course of one year.[37] These studies suggest that a dosage of 25µg orally disintegrating desmopressin before going to sleep at night appears to be optimal for women, whereas men may benefit from 50µg.[36]

A once-daily, low-dose, gender-specific formulation of desmopressin has recently been developed (Box 4).[39] These formulations limit the mean antidiuretic action of desmopressin to three to five hours during the nightly sleep period, and thereby reduce the risk of clinically significant hyponatraemia (*ie* serum Na^+ concentration <130mmol/L), a treatment-limiting adverse event associated with higher doses of desmopressin. Hyponatraemia is most frequent in patients aged >65 years and with low baseline serum sodium concentration. Fluid intake should be limited from one hour before until eight hours after administration of desmopressin. Treatment without concomitant reduction of fluid intake may lead to prolonged fluid retention and/or hyponatraemia with or without accompanying warning signs and symptoms (headache, nausea/vomiting, weight gain and, in severe cases, convulsions or even coma).[39]

Treatment with a V_2 agonist is only useful in those patients who have idiopathic nocturnal polyuria with excessive water diuresis, which is an indication of suppressed vasopressin.[41]

Box 3. Recommended lifestyle modification

- Avoid drinking alcoholic or caffeinated beverages in the evening
- Reduce total fluid intake to less than 2L/d when comorbidities allow for it
- Restrict fluids a couple of hours before going to sleep
- Empty bladder before going to bed
- Elevate legs over the chest level two to three hours prior to bedtime (patients with nocturnal polyuria due to congestive heart failure or peripheral oedema)
- Change the intake of diuretics to mid to late afternoon rather than just after arising or immediately prior to retiring (for patients on diuretics)*
- Moderate physical exercise and pelvic floor exercises, if indicated
- Weight loss if overweight/obese

*Be aware that the timing is dependent on the specific diuretic drug, which has, for example, a serum half-life of approximately 1.5 hours for furosemide but approximately 3.5 hours for torasemide.

Other pharmacological agents

Other pharmacological agents have also been used in the treatment of nocturia, including alpha-1 blockers, 5-alpha reductase inhibitors and antimuscarinics. Although most studies documented a significant reduction of nocturnal voiding frequency, the clinical impact is only modest with these agents.[29,30]

All studies on alpha-1 blockers have been conducted in the context of LUTS/benign prostatic obstruction management.[25,42] While treatment of nocturia with alpha-1 blockers and/or antimuscarinics has been associated with statistically significant improvements in symptoms, the clinical significance of the reported changes is debatable.[29,42,43] The same applies for the treatment of nocturia in men with 5-alpha reductase inhibitors with or without alpha-1 blockers, phosphodiesterase type 5 inhibitors or plant extracts.[44–47] The majority of studies on antimuscarinics have been conducted in the context of OAB syndrome management.[38] In some patients, multiple treatment options should be combined to provide the most effective treatment. Prospective studies have demonstrated that the addition of low-dose desmopressin to an alpha-1 blocker (various types) in men with LUTS/BPH and to an antimuscarinic (tolterodine) in women with OAB is an effective and well tolerated treatment for nocturia.[39,48–50] The number of nocturnal voids decreased to a greater extent with combination treatment than with alpha-1 blocker/antimuscarinic monotherapy, while overall tolerability remained similar.[39,48–50]

Box 4. Recommended daily dose of desmopressin orally disintegrating tablet[39,40]

Women	25µg daily, one hour before bedtime, administered without water
Men	50µg daily, one hour before bedtime, administered without water

- Fluid intake should be limited to a minimum, from one hour before until eight hours after administration of desmopressin
- In patients aged ≥65 years, serum sodium should be monitored before starting treatment, in the first week of treatment (four to eight days) and again at one month after starting treatment

Other interventional options

Based on the available evidence, the ICUD committee considered that bladder outlet obstruction-reducing procedures may improve nocturia in some patients with voiding LUTS and bladder outlet obstruction who fail medical therapy and who are good surgical candidates.[33] Surgery for relief of bladder outlet obstruction is not indicated for management of patients whose primary complaint is nocturia. Comprehensive evaluation of the cause(s) of nocturia is essential before contemplating a surgical approach.[33]

Nocturia is a common problem in patients with obstructive sleep apnoea (OSA). Meta-analysis of five clinical studies indicates that continuous positive airway pressure (CPAP) may be an effective treatment for reducing nocturia associated with OSA and improving the QoL of patients with nocturia.[51] In this study, nocturia ($p<0.00001$) and night-time urine volume ($p<0.00001$) were significantly decreased after CPAP treatment.[51]

MEDICATION ADHERENCE

Adherence to medication is important in nocturia care to achieve improved patient functioning and QoL. To facilitate adherence, it is important to:[52]

- Educate the patient regarding available treatment options and discuss preferences
- Provide advice on lifestyle modifications
- Communicate the risks and benefits of treatment and the proper use of medication
- Involve the patient in the decision-making process.

CONCLUSIONS

Nocturia is a multifactorial and often complex medical condition that affects men and women equally and is often overlooked. Nocturia can have a negative impact on sleep and work productivity, and can increase morbidity

and mortality. The FVC is an essential evaluation tool that can facilitate accurate identification of the potential multiple causes of nocturia in an individual patient, providing evidence by which the aetiology of nocturia can be categorised into one or a combination of categories of sleep disorders, nocturnal polyuria, global polyuria and reduced bladder capacity.

The management of nocturia should be based on an approach that targets the underlying cause(s). Management should start with behavioural treatments and lifestyle interventions. If these fail to bring adequate relief, then treatment with pharmacological agents, such as desmopressin, is indicated. Patients whose nocturia remains bothersome should be referred to the appropriate specialist depending on the primary underlying cause identified.

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Frequency-volume chart

Day 1 (..../..../....)					
Time of waking up:			Time of going to sleep:		
Time	Drinks		Urine	Accidental leaks	
	What kind?	How much?	How urgent?	How much?	Y/N
Example	Coffee	2 cups	1–3 (3=most urgent)	25ml	Yes
Please do not include here first morning void					
6–7am					
7–8am					
8–9am					
9–10am					
10–11am					
11am–12pm					
12–1pm					
1–2pm					
2–3pm					
3–4pm					
4–5pm					
5–6pm					
6–7pm					
7–8pm					
8–9pm					
9–10pm					
10–11pm					
11pm–12am					
12–1am					
1–2am					
2–3am					
3–4am					
4–5am					
5–6am					
Morning void in ml (after waking) at day 2:					
Total 24 hours					
Total night					

Day 2 (..../..../....)					
Time of waking up:			Time of going to sleep:		
Time	Drinks		Urine	Accidental leaks	
	What kind?	How much?	How urgent?	How much?	Y/N
Example	Coffee	2 cups	1–3 (3=most urgent)	25ml	Yes
Please do not include here first morning void					
6–7am					
7–8am					
8–9am					
9–10am					
10–11am					
11am–12pm					
12–1pm					
1–2pm					
2–3pm					
3–4pm					
4–5pm					
5–6pm					
6–7pm					
7–8pm					
8–9pm					
9–10pm					
10–11pm					
11pm–12am					
12–1am					
1–2am					
2–3am					
3–4am					
4–5am					
5–6am					
Morning void in ml (after waking) at day 3:					
Total 24 hours					
Total night					

Day 3 (..../..../....)					
Time of waking up:			Time of going to sleep:		
Time	Drinks		Urine	Accidental leaks	
	What kind?	How much?	How urgent?	How much?	Y/N
Example	Coffee	2 cups	1–3 (3=most urgent)	25ml	Yes
Please do not include here first morning void					
6–7am					
7–8am					
8–9am					
9–10am					
10–11am					
11am–12pm					
12–1pm					
1–2pm					
2–3pm					
3–4pm					
4–5pm					
5–6pm					
6–7pm					
7–8pm					
8–9pm					
9–10pm					
10–11pm					
11pm–12am					
12–1am					
1–2am					
2–3am					
3–4am					
4–5am					
5–6am					
Morning void in ml (after waking) at day 4:					
Total 24 hours					
Total night					

Prescribing Information: NOCDURNA® 25 and 50 micrograms oral lyophilisate. Please consult the full Summary of Product Characteristics before prescribing.
Name of Product: NOCDURNA® 25 micrograms oral lyophilisate; NOCDURNA® 50 micrograms oral lyophilisate. **Composition:** 25 or 50 micrograms of desmopressin (as lyophilisate). **Indications:** Symptomatic treatment of nocturia due to idiopathic nocturnal polyuria in adults. **Dosage:** Women 25 microgram daily, men 50 microgram, daily one hour before bedtime administered sublingually without water. **Contraindications:** Hypersensitivity to the active substances or to any of the excipients, habitual or psychogenic polydipsia, known or suspected cardiac insufficiency or other conditions associated with fluid overload moderate and severe renal insufficiency, known history of hyponatremia, syndrome of inappropriate ADH secretion (SIADH). **Special Warnings and Precautions:** Not recommended in patients with cardiovascular or other medical conditions associated with fluid overload. Fluid intake must be limited to a minimum from 1 hour before until 8 hours after administration. Patients 65 years and older should have their serum sodium monitored before initiating the treatment, in the first week of treatment and at one month after treatment initiation. Discontinue NOCDURNA® if serum sodium level falls below the lower limit of normal. Use with caution in patients with conditions characterized by fluid and/or electrolyte imbalance. Fluid restriction and more frequent monitoring of serum sodium must be taken in case of concomitant treatment with drugs known to induce SIADH. Caution is required in cases of cystic fibrosis, coronary heart disease, hypertensions, chronic renal disease and pre-eclampsia. Ensure patients taking lithium do not have early-stage lithium-induced nephrogenic diabetes insipidus. **Side Effects:** Dry mouth, headache, dizziness, diarrhoea, nausea. *Uncommon:* cases of constipation, abdominal discomfort, fatigue, peripheral oedema. Treatment with desmopressin without concomitant reduction of fluid intake may lead to water retention/hyponatraemia with or without accompanying warning symptoms of headache, nausea/vomiting, decreased serum sodium, weight gain and in serious cases convulsions. Consult the full Summary of Product Characteristics for further information about side effects. **Basic NHS Prices:** Carton containing 30 oral lyophilisates in blister strips. 30 x 25 micrograms £15.16. 30 x 50 micrograms £15.16. **Marketing Authorisation Number:** 50 micrograms 03194/0119. 25 micrograms 03194/0118. **Marketing Authorisation Holder:** Ferring Pharmaceuticals Ltd., Drayton Hall, Church Road, West Drayton, UB7 7PS. **Legal Category:** POM.
Date of Preparation of Prescribing Information: August 2016. All trademarks registered to Ferring. **PI approval code:** NOQ/2109/2016/UK.

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