

Clinical review

Managing nocturia

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Introduction

Nocturia, or frequent urination at night time, is a common but poorly reported and largely misunderstood urological disorder in adults.^{1 2} Although many people awaken during the night to urinate, the condition has received little attention in the medical literature, and definitions vary widely. The International Continence Society defines nocturia as two or more night time voids. In its simplest terms, nocturia refers to urination at night and entails some degree of impairment, with urinary frequency often considered excessive and disruptive. However, excessive urination may refer to either the volume of urine voided or the number of trips to the toilet, as normal frequency and volume for nocturnal urination have been poorly defined among all age groups.^{3 4} With no accepted distinction between normal and abnormal urination, doctors tend to overlook nocturia as a possible source of medical problems associated with the resultant loss of sleep, and patients tend not to report the condition to their doctors until it becomes unbearable or their quality of life during daytime hours is severely compromised.⁵ Nocturia has a role in numerous aspects of people's health and wellbeing, contributing to fatigue, memory deficits, depression, increased risk of heart disease, gastrointestinal disorders, and, at times, traumatic injury through falls. Adequate, restful sleep is important to everyone, regardless of age. Our entire way of life, our health, happiness, and ability to function at home and at work suffer from inadequate rest. Evidently nocturia is more complex and important a condition than recognised so far. Identifying nocturia, determining its causes, and treating it effectively are keys to improving patients' quality of life.

Sources

We searched Medline for 1980-2003 by using the key words "nocturia" and "nocturnal polyuria." We selected 22 references for this review.

Causes

In general nocturia affects older people more than younger adults, and those aged 65 or greater are more likely to experience a need to urinate at night. Many people with nocturia, especially elderly men, also experience concomitant lower urinary tract problems, such as frequency, urgency, weak stream, and incontinence—symptoms often attributed to benign prostatic obstruction. Age, childbirth, and menopause are often

Summary points

Nocturia, or frequent night time urination, is a common but poorly reported and largely misunderstood urological disorder in adults

Nocturia has a role in numerous aspects of people's health and wellbeing

Multiple factors may cause nocturia in both men and women

Identifying nocturia, determining its causes, and appropriating effective treatment are keys to improving patients' quality of life

A complete history and physical examination must be conducted

Treatment options for nocturia depend on the diagnosis and underlying cause(s)

Sacral neuromodulation is a new, minimally invasive surgical technique for patients in whom pharmacotherapy has failed and non-surgical or surgical interventions have proved unsuccessful

Although evidence of its efficacy is preliminary, the procedure has been successfully implemented in numerous patients, notably reducing the degree of urgency and total number of voids

suggested contributors to nocturia in women.^{5 6} Multiple factors may cause nocturia in both men and women; these include behavioural patterns, diuretic medications, caffeine, alcohol, or excessive fluids before bedtime, and pathological conditions, such as prostatic disease, diabetes mellitus or diabetes insipidus, obstruction of the lower urinary tract, anxiety, or sleep disorders.^{7 8} The condition may also result from stroke, cardiovascular disease, peripheral oedema, and myeloneuropathy.⁹

Effects

Regardless of aetiology, nocturia is a condition demanding further study, since one primary effect is sleep disturbance, which is bothersome and far reaching, affecting physical health and mental wellbeing. It is

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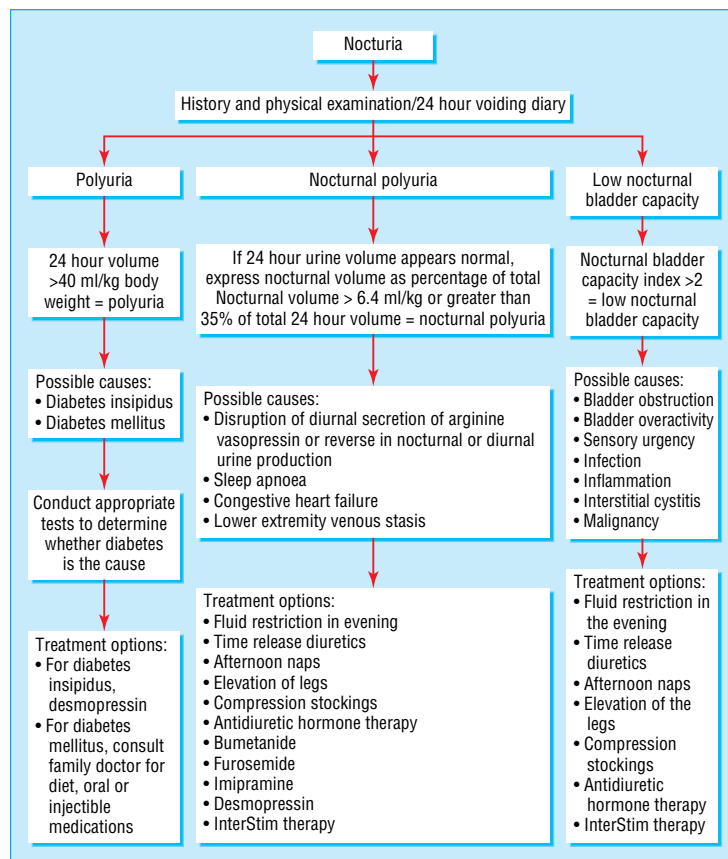


Fig 1 Algorithm for the definition and treatment of nocturia

generally accepted that adults require seven to eight hours of sleep per night to refresh and restore the body, yet studies have shown that, as we age, insufficient sleep becomes more common and quality of sleep diminishes.¹⁰ Several studies of both men and women experiencing nocturia indicate that the condition is indeed bothersome, regardless of sex or age. Jollys et al conducted a study among men experiencing benign prostatic obstruction. Participants indicated that nocturia at least twice nightly was a bothersome symptom, although not reported as often as dribbling, hesitancy, or urgency.¹¹ Another study of UK women older than 19 showed that, for 62.6% of participants, nocturia twice during the night was “at least a bit of a problem.”¹² Finally, in a study of the management of chronic health conditions by elderly people living in the community, 72% of participants suffered interruptions to night time rest due to urination, and comments regarding bothersomeness ranged from “quiet resignation” to “annoyance and despair.”¹⁷ Yet the simple annoyance of disturbed sleep is not the most notable effect of nocturia; insufficient sleep has been linked with depression, alterations in mood, and excessive daytime fatigue, which affect motivation and job performance and increase the likelihood of traumatic injury (most commonly hip fractures) from falling. A high proportion of falls among elderly hospital patients occurs because of toileting and trips to and from the bed.⁷

Assessment

Nocturia can be a debilitating problem for many sufferers, and initial attempts at self management through

fluid restriction are often futile and increase the patient's risk of dehydration. Recognising the disorder and determining its causes are therefore crucial to treating it effectively. A treatment algorithm serves as a valuable tool by which the doctor can make an accurate diagnosis of the condition (fig 1). Patients often present to the doctor with indirect symptoms, such as insomnia, excessive sleepiness during daytime, depression, and mood changes resulting from insufficient sleep.^{13 14} A complete history and physical examination must be conducted, taking into consideration various aspects of the patient's health, such as presence of sleep disorders, urinary problems, fluid intake, medications, and heart disease. Most important is a 24 hour voiding diary, in which each urinary void is entered with corresponding time and amounts voided (ml), and degree of urgency (1 = mild to 5 = severe). The patient may then be categorised as having one of three general categories of nocturia: nocturnal polyuria, low nocturnal bladder capacity, or mixed nocturia (a combination of the preceding two categories).

Nocturnal polyuria

Nocturnal polyuria was first defined by Asplund in 1995 as increased nocturnal output of urine, yet parameters to quantify urinary overproduction have been established only recently, with some researchers characterising the condition as night time urine volume in excess of 6.4 ml/kg.⁸ Others define it as nocturnal output exceeding one third of one's total daily urine output¹⁵; and still others consider nocturnal urine overproduction as a function of bladder capacity, determined via a recently developed nocturia index, which is defined as nocturnal urine volume divided by functional bladder capacity.¹⁶

$$\frac{\text{Nocturnal urine volume}}{\text{functional bladder capacity}} = \text{nocturia index}$$

Functional bladder capacity is defined as the single largest volume voided and recorded in one's voiding diary. If the nocturia index is greater than 1, nocturnal polyuria (excessive urination at night time) results, as nocturnal urine output exceeds the bladder's maximal storage capacity. The condition may arise in some patients from a reverse in nocturnal or diurnal urine production, resulting from a disruption of the body's diurnal secretion of arginine vasopressin, a hormone that increases resorption of water from the renal tubule, reducing volumes of concentrated urine. A possible explanation for this disruption is that persistent, long term urinary tract obstruction may create pressure induced lesions in the renal system, interfering with normal circadian renal handling of sodium by decreasing diurnal sodium excretion.⁸ Patients with respiratory diseases such as sleep apnoea may also experience nocturnal polyuria due to increased renal sodium and water excretion brought about by raised concentrations of atrial natriuretic peptide.¹⁷ Studies have shown that apnoeic respiratory obstruction creates hypoxia induced pulmonary vasoconstriction, increasing right atrial transmural pressure and raising peptide concentrations.¹⁸ Polysomnographic studies are recommended for patients with nocturnal polyuria who are also suspected of



Fig 2 InterStim sacral neuromodulation device

having obstructive sleep apnoea, especially those with obesity, asthma, hypertension, and adult onset diabetes mellitus. Nocturnal polyuria may also result from third spacing of fluid in the lower extremities caused by right congestive heart failure and venous stasis in the lower extremities.¹⁷ Detailed diagnostic tests such as an echocardiogram and nuclear testing should be completed in conjunction with a comprehensive history and physical examination for patients at risk of cardiac disease.

Low nocturnal bladder capacity

Many patients with nocturia have a combination of nocturnal polyuria and low nocturnal bladder capacity. Notably low bladder capacity (nocturnal bladder capacity index >2) may result from bladder obstruction, bladder overactivity, sensory urgency, or primary bladder conditions such as infection, inflammation, interstitial cystitis, or malignancy.¹⁷ Recognising and treating the underlying disorder would be expected to alleviate or at least ameliorate symptoms of nocturia.

Treatment options

Depending on the diagnosis and underlying cause(s), treatment options for nocturnal polyuria may include restriction of fluids in the evening, time release diuretics,¹⁹ afternoon naps, elevation of the legs, compression stockings, and treatment with antidiuretic hormone. Accumulation of fluid in the lower extremities in some patients may eliminate simple fluid restriction as an effective alternative. However, compression stockings and late afternoon naps with the legs elevated may reduce fluid build up and help alleviate nocturnal polyuria. Swelling in the legs or presacral area may also improve with diuretics, although this treatment must be administered well before bedtime. Because diuretics act within two hours of administration, medications taken later in the evening may actually exacerbate the problem. Bumetanide, furosemide, and, recently, imipramine have all proved effective in reducing polyuria.²⁰ Desmopressin has also reduced or eliminated nocturia in patients with diabetes insipidus, autonomic dysfunction, and Parkinson's disease. For patients with benign prostatic enlargement, treatment with melatonin, a pineal gland hormone, which is a prime physiological determinant of circadian rhythms, may be an effective option.²¹ Because nocturnal production of the hor-

none is impaired in older adults, administration of melatonin can restore a normal circadian rhythm of micturition and improve sleep. In fact, men treated with 2 mg of melatonin generally experience a 10% reduction in episodes of nocturia.²¹ For patients in whom pharmacotherapy has failed and non-surgical or surgical interventions have proved unsuccessful, a new, innovative, and minimally invasive surgical technique for urgency, urge incontinence, and nocturia is sacral neuromodulation. Although evidence of its efficacy is preliminary, the procedure has been used successfully in several patients, notably reducing the degree of urgency and total number of voids.²² In the recent past only experimental or low yielding surgical alternatives were available, with success rates below 30%. But now a lightweight (50 g), implantable device, InterStim (fig 2), which stimulates the third sacral nerve, has achieved one year success rates approaching 85% for controlling urgency, urge incontinence, and nocturia.²³ This is quite promising as these patients tend to be those in whom all traditional medical treatments have failed, and, typically, successful treatment has been difficult to obtain or sustain. Sacral neuromodulation is performed as a day

Additional educational resources

Websites for patients

British United Provident Association. Incontinence in women (http://hcd2.bupa.co.uk/fact_sheets/html/Urinary_incontinence_women.html)—provides basic, simple to read information for women, regarding symptoms and causes of incontinence, descriptions of various types of incontinence, and options for treatment.

50+Health, Incontinence (www.50plushealth.co.uk/index.cfm?articleid=2079)—presents a wealth of information regarding incontinence, statistics of the condition among men and women, options for management and treatment, and links to detailed pages on urgency and the various types of incontinence. Colourful sketches and bulleted lists make the site attractive and easy to understand. A discussion forum allows visitors to share their experiences with others.

eMedicine Consumer Health, bladder control problems (www.bladdercontrol.e-medicinehealth.com/nocturia.htm)—offers information about incontinence, resultant health conditions, causes (in both men and women), tests to determine the presence of incontinence, treatment options, self care suggestions, and addresses/phone numbers of support groups and counselling agencies.

Pharmacia. Who has nocturia? (www.bladderinfo.com/problems/nocturia.htm)—describes the prevalence of bladder conditions and offers information about normal bladder function and causes, symptoms, risk factors, and treatment options for various bladder disorders. An interactive quiz helps visitors determine whether they have a bladder condition that requires medical intervention.

Medtronic. InterStim therapy (www.interstim.com)—describes treatment with the InterStim device—a new neurostimulation device for patients who have failed or could not tolerate more conservative treatments for urgency frequency, urge incontinence, or urinary retention—and offers a link to doctors nationwide who perform the procedure.

Websites for doctors

Pharmacia. Detrol LA (www.detrol.com/hcp/index.asp)—provides guidance for the screening and diagnosis of overactive bladder and information on treatment using the drug. Pages describing clinical effectiveness and patient assessment tools are most helpful.

Medtronic. InterStim therapy (www.interstim.com)—provides doctors' indications for treatment, information about clinical trials, and education and certification opportunities.

National Association for Continence (www.nafc.org/site2/index.html)—offers information about causes, methods of prevention, and treatment options for incontinence and provides updates about the latest publications and conferences on the topic.

A patient's success story

Janet Murray, a guard in a correctional facility, is a 42 year old white woman with an 8 year history of frequency, urgency, and nocturia. Before treatment, she voided up to 25 times in a 24 hour period; four to six times per night. Janet could remember experiencing only one normal night's rest after the age of 40. She was concerned that her impaired sleep was placing her job at risk because of drowsiness during the day shift and urinary frequency (aggravated by a lack of readily available lavatory access) during the night shift. She had failed bladder training, timed voiding, biofeedback, and maximum doses of anticholinergic medications, including Ditropan XL, Detrol LA, and imipramine. Urodynamics showed an unstable bladder. Luckily, Janet was deemed a candidate for a new method of neuromodulation with an implantable device called InterStim. Similar to a cardiac pacemaker but stimulating the third sacral nerve, InterStim has achieved remarkable results, with a reduction in episodes of nocturia of more than 60%. One year after implantation, Janet reports having had an immediate and sustained improvement in her frequency and nocturia. She now voids a total of six to eight times in 24 hours, with no episodes of nocturia. Her job is no longer at risk, and her quality of life has improved substantially.

procedure, entailing the implantation of a temporary device with a neuromodulation unit only slightly larger than a pager attached to the patient's regular pant belt. This stage 1 procedure is performed under local anaesthesia and takes less than 45 minutes. If the patient's symptoms improve by more than 50%, a permanent device is implanted in either buttock with a 6 cm incision. The device can be programmed via an extracorporeal handheld device for increases or decreases in power magnitude. The effects on nocturia have been remarkable, with a reduction of more than 60% in episodes of nocturia, even in patients taking diuretic medication. Adverse events such as pain at the implant site, lead migration, infection or skin irritation, or technical or device related problems are possible in up to one third of patients, and contraindications such as benign prostatic hypertrophy, cancer, or urethral stricture may exclude some patients from candidacy for the procedure²⁴; in general, however, sacral neuromodulation is an effective, safe, and reversible treatment and offers an important new option²² for patients with symptoms of urgency, urge incontinence, and nocturia.

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- Middlekoop 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* 1996;51:M108.
- Asplund R, Aberg HE. Micturition habits of older people. Voiding frequency and urine volumes. *Scand J Urol Nephrol* 1992;26:345.
- Shah PJR. *The assessment of patients with a view to urodynamics. Urodynamics: principles, practice and application*. New York: Churchill Livingstone, 1994.
- Hennessy CH, Shen JKM. Sources of unreliability in the multidisciplinary team assessment of the elderly. *Eval Rev* 1986;10:178.
- Umlauf MG, Goode S, Burgio K. Psychosocial issues in geriatric urology: problems in treatment and treatment seeking. *Urol Clin North Am* 1996;23:127.
- Fultz NH, Herzog AR. Epidemiology of urinary symptoms in the geriatric population. *Urol Clin North Am* 1996;23:1.
- Barker JC, Mitteness LS. Nocturia in the elderly. *Gerontologist* 1988;28:99.
- Matthiesen TB, Rittig S, Norgaard JP, Pedersen EB, Djurhuus JC. Nocturnal polyuria and natriuresis in male patients with nocturia and lower urinary tract symptoms. *J Urol* 1996;156:1292.
- Sullivan MP, Yalla SV. *Alternate methods in the treatment of benign prostatic hyperplasia*. New York: Springer, 1993.
- Broman JE, Lundh LG, Hetta J. Insufficient sleep in the general population. *Neurophysiol Clin* 1996;26:30.
- Jolleys JV, Donovan JL, Nanchahal K, Peters TJ, Abrams P. Urinary symptoms in the community: how bothersome are they? *Br J Urol* 1994;74:551.

- Swithinbank LV, Donovan J, James MC, Yang Q, Abrams P. Female urinary symptoms: age prevalence in a community dwelling population using a validated questionnaire. *NeuroUrol Urodyn* 1998;16:432.
- Hetta J, Rimon R, Almqvist M. Mood alterations and sleep. *Ann Clin Res* 1985;17:252.
- Lindberg E, Janson C, Gislason T, Bjornsson E, Hetta J, Boman G. Sleep disturbances in a young adult population: can gender differences be explained by differences in psychological status? *Sleep* 1997;20:381.
- Saito M, Kondo A, Kato T, Yamada Y. Frequency-volume charts: comparison of frequency between elderly and adult patients. *Br J Urol* 1993;72:38.
- Weiss JP, Blaivas JG, Stember DS. Nocturia in adults: etiology and classification. *NeuroUrol Urodyn* 1998;17:467.
- Weiss JP, Blaivas JG. Nocturia. *J Urol* 2000;163:5-12.
- Krieger J, Petiau C, Sforza E, Delanoe C, Hecht MT, Chamouard V. Nocturnal pollakiuria is a symptom of obstructive sleep apnea. *Urol Int* 1993;50:93-7.
- Pederson PA, Johansen PB. Prophylactic treatment of adult nocturia with bumetanide. *Br J Urol* 1988;62:145.
- Hunsballe JM, Rittig S, Pedersen EB, Olesen OV, Djurhuus JC. Single dose imipramine reduces nocturnal urine output in patients with nocturnal enuresis and nocturnal polyuria. *J Urol* 1997;158:830.
- Drake MJ, Mills IW, Noble JG. Melatonin pharmacotherapy for nocturia in men with benign prostatic enlargement. *J Urol* 2004;171:1199-202.
- Hassouna MM, Siegel SW, Nyeholt AA, Elhilali MM, van Kerrebroeck PE, Das AK, et al. Sacral neuromodulation in the treatment of urgency-frequency symptoms: a multicenter study on efficacy and safety. *J Urol* 2000;163:1849-54.
- Spinelli M, Giardiello G, Gerber M, Arduini A, van den Hombergh U, Malaguti S. New sacral neuromodulation lead for percutaneous implantation using local anesthesia: description and first experience. *J Urol* 2003;170:1905-7.
- Medtronic. What is InterStim therapy? www.interstim.com (accessed 31 Mar 2004).

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Corrections and clarifications

Minimally invasive parathyroidectomy

Late insertion of authors' affiliations in this editorial led to some confusion over authorship, which resulted in us adding a third, non-existent, author, T S Reese (10 April, pp 849-50). The article had only two authors, F Fausto Palazzo and Gregory P Sadler, both of whom worked at John Radcliffe Hospital in Oxford (as specialist registrar in endocrine surgery and consultant endocrine surgeon respectively) at the time of writing the editorial. F Fausto Palazzo is now T S Reeve fellow in endocrine surgery, Royal North Shore Hospital, Sydney, Australia. The authorship has been amended on bmj.com.

Why do doctors use treatments that do not work?

The authors of this editorial, Jenny Doust and Chris Del Mar, prompted by a rapid response, have alerted us to an error in their editorial (28 February, pp 474-5). In the fourth paragraph, they misquoted reference 9. The authors had written that flecainide for the treatment of supraventricular tachycardia makes the electrocardiogram look normal, whereas the trial cited investigated use of flecainide for ventricular tachycardia.

This week in the BMJ: Three days of amoxicillin are enough for non-severe pneumonia

We inadvertently omitted the word "excess" in this summary paragraph for the paper by the ISCAP Study Group ("Three day versus five day treatment with amoxicillin for non-severe pneumonia in young children: a multicentre randomised controlled trial," 3 April, pp 791-4). The fourth sentence should read: "Clinical failure was more likely with non-adherence to treatment at day 5, an excess respiratory rate of > 10 breaths/minute, and infection with respiratory syncytial virus." Although the reader who alerted us to this error claimed that the slip prompted him to read the whole article, introducing errors to attract readers is not a strategy that we are planning to adopt.