Nocturia

Nocturia is a common and often distressing condition with increasing incidence in the elderly. It has multiple causes and a focused history taking and physical examination will help to establish the underlying diagnosis. A voiding chart is a useful tool in investigation and also for assessing response to treatment. A multifaceted management approach can help to reduce the number of episodes of nocturia resulting in a significant improvement in quality of life.

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Nocturia, literally waking at night to void urine, is a common symptom with multiple aetiologies. Nocturia is clinically defined as the regular occurrence of two or more night time voids that leads to disruption of a person's quality of life.[1] It is distinct from nocturnal eneuresis (bed wetting). Nocturia is often poorly reported but is more likely to be mentioned by a patient if there are three or more episodes of voiding each night. [2]

Nocturia is more prevalent with advancing age.[3] In people less than 50 years old, nocturia is more common in women than men primarily due to obstetric and pelvic floor related bladder dysfunction. In people over 60 years old the sex ratio reverses with more men than women having nocturia. It has been reported that in men over 70 years old nearly 50% have twice nightly or greater nocturia.[4]

Nocturia is not a trivial symptom as it is consistently associated with poor quality of life ratings.[5] Nocturia-induced sleep disruption has been linked to increased rates of depression,[6] memory deficits, fatigue, work absenteeism, falls[7] and increasing all cause mortality.[8] Nocturia is poorly reported until it has become unbearable.[9]

Normal bladder filling is dependent on the unique property of bladder wall elasticity, which allows an increase in volume at a pressure lower than that of the bladder neck and urethra. If not for this, urinary incontinence would be the norm. Bladder emptying is dependent on the integrity of a complex neuromuscular network that causes relaxation of the urethral spincter just before bladder muscle (detrusor) contraction. Thus an intact neural pathway from the brain via spinal cord to sacral segments S2–S4 and peripheral nerves is vital for voluntary control of micturition.

It is important to thoroughly assess, examine and investigate patients with nocturia as this symptom may be a flag that alerts clinicians to serious but potentially treatable underlying disorders.

Differential diagnosis

A variety of conditions may trigger nocturia and some of these disorders

Key points

- Nocturia is clinically defined as the regular occurrence of two or more night time voids that leads to disruption of a person's quality of life.
- Nocturia is poorly reported until it has become unbearable.
- It may be a flag that alerts clinicians to serious but potentially treatable underlying disorders.
- It is important to obtain information about any associated urinary incontinence, lower urinary tract obstructive symptoms and bladder irritative problems.

may co-exist in an individual patient. Nocturia is more likely if any of the following are present:

- Polyuria
- Nocturnal polyuria
- Lower urinary tract dysfunction leading to low volume voiding
- Neurological disorders affecting bladder function
- Sleep disorders.

Polyuria

This is day and night time polyuria (defined as urine volume > 40 mls/kg/24 hrs). It may be due to excess fluid intake (including alcohol); an osmotic diuresis due to diabetes mellitus; or an inability to form concentrated urine resulting in obligate high 24-hour urine volumes. A diseased kidney may be very resistant to anti-diuretic hormone (also known as arginine vasopressin) and nocturia can be a symptom of chronic kidney disease. Acquired resistance to anti-diuretic hormone may also result from chronic lithium treatment leading to a state of diabetes insipidus with symptoms of polyuria and nocturia.

Nocturnal polyuria

Nocturnal polyuria is the commonest cause of nocturia (defined as normal 24-hour urine volume but with an increased nocturnal urine volume to >35% of daily total). Normally there is a decrease in urine output during the night time relative to daytime. This is primarily due to higher night time levels of anti-diuretic hormone (ADH), which targets receptors on the distal tubule of the nephron to reabsorb water and produce a lower volume of more concentrated urine. This physiological diurnal variation in ADH release is absent in many older people.[10] In normal health there is also a decreased solute excretion at night time and this is another reason for a relatively low nocturnal urine output. In patients with heart failure or other oedematous disease states there is nocturnal redistribution of oedema fluid and solutes which leads to nocturnal polyuria and a solute diuresis.

Lower urinary tract dysfunction

A low nocturnal bladder capacity may be associated with lower urinary tract obstruction or bladder irritation. Bladder outlet obstruction is common in older men with prostatic disease and can lead to chronic urinary retention with limited capacity to store any additional nocturnal urine volume. Associated "obstructive" symptoms such as hesitancy, poor stream and terminal dribbling can help to identify this particular cause of nocturia. Bladder irritation can occur due to cystitis, urinary tract infection or malignancy. This can result in detrusor muscle hyperactivity and associated symptoms of urgency, daytime frequency and urge incontinence. Increasing age has been associated with reduced bladder volume and it is unclear whether this is due to detrusor hyperactivity itself or simply related to ageing.[11]

Neurological disorders

Urinary retention resulting in frequency, overflow incontinence or nocturia may be caused by a serious neurological problem. Urgent disorders to recognise include cord compression[12] and cauda equina syndrome.[13] A neurological cause (rather than bladder outlet obstruction) should always be considered in the differential diagnosis for urinary retention especially in women and men under 60 years old. Autonomic neuropathy associated with diabetes mellitus can result in a neuropathic bladder with urinary retention that can present with nocturia and overflow incontinence. Other neurological conditions that can cause nocturia include multiple sclerosis and Parkinson's disease.[14]

Sleep disorders

Obstructive sleep apnoea (OSA),[15] restless leg syndrome and periodic limb movements at night are frequently associated with nocturia. The patient with a sleep disorder may attribute the need to pass urine as the reason for waking. OSA may also cause nocturnal polyuria as negative intra-thoracic pressures can result in elevated atrial naturetic peptide levels resulting in increased night time sodium and water excretion. Depression has also been associated with nocturia possibly linked to poor sleep patterns.

History and clinical examination

Confirmation of nocturia should include two important questions. The first about the frequency of night time voiding and second, about the disruption it is causing to their normal day-to-day activities.

Once nocturia is confirmed, it is important to obtain information about any associated urinary incontinence, lower urinary tract obstructive symptoms and bladder irritative problems. The patient should be asked about the pattern and type of fluid intake. It is important to note if any comorbid medical conditions could be contributing to nocturia such as chronic kidney disease, heart failure or obstructive sleep apnoea. Medication should be reviewed to establish if diuretics or lithium are

implicated. Patients may habitually be consuming large amounts of fluid particularly in the evening and it is important this is included in the management plan. Both caffeine (causing polyuria and detrusor overactivity) and alcohol (diuretic effect) should be avoided in the evening. The timing of twice daily diuretic dose should be revised, moving the second dose to midday. It is also important to ask about neurological or spinal symptoms such as back pain, sphincter disturbance, sexual dysfunction, saddle area sensory loss, abnormal gait, limb weakness or limb sensory loss.

Clinical examination

A thorough examination keeping in mind some of the rarer but urgent clinical diagnoses is important. If on abdominal exam an enlarged bladder is detected or suspected then a rectal examination for prostate enlargement (men), assessment for saddle sensory loss (perianal sensory loss or "numb bum") and testing of anal reflex are appropriate. Other features to assess include:

- Cardiovascular: examine for volume overload (oedema, raised JVP, pulmonary oedema) and orthostatic hypotension (which may impact on subsequent alpha blocker prescribing)
- Renal: dipstick urinalysis
- Neurological: evaluation for spinal cord lesions.

Investigations

Urine analysis

Dipstick urinalysis can provide information on urine concentration (specific gravity); diabetes (glucose); urine infection (nitrites and leucocytes); and kidney disease (protein +/- blood). If infection is suspected urine culture should be performed.

Blood tests

Serum glucose, serum creatinine and electrolytes should be checked in all patients. Prostate specific antigen (PSA) level in men with other lower urinary tract symptoms may be considered.

24 hour urine volume and voiding chart

Sleep and wake time should be recorded. A good record can help determine the type of nocturia (ie. low volume bladder void, increased nocturnal polyuria, or both), bladder capacity and also help in assessing treatment response. If 24-hour urine volume is more than expected, a record of fluid intake could be helpful. This should note time of fluid intake, type and amount of fluid, time of void and amount voided.

Urodynamic studies

A post void residual bladder volume could be tested either by ultrasound or by catheterisation. A bladder volume of less than 50mls is considered as adequate emptying while a residual volume greater than 200mls would warrant further urological evaluation for bladder outlet obstruction. Urinary peak flow rates can also be measured and generally a value greater than or equal to 15mls/second makes bladder outlet obstruction less likely.

Treatment

Although complete resolution of symptoms is infrequent, it is possible to reduce the number of episodes of nocturia and help improve the quality of life for patients.

General measures

Multiple lifestyle adjustments to the total volume of fluid intake, reduction in evening diuretic, avoiding stimulants such as caffeine and alcohol, use of compression stockings for peripheral oedema, optimising treatment of comorbidities and timing of specific medications (ie avoiding diuretics at bedtime) can help. None of these interventions in isolation have proven beneficial in reduction of nocturia but may be useful as part of an overall management strategy.[16]

Specific measures

Pelvic floor exercises in women have proven benefit in reduction of nocturia episodes.[17,18]

Pharmacological therapies directed towards treatment of bladder overactivity, bladder outlet obstruction and nocturnal polyuria might help reduce nocturia episodes.

Alpha-blockers have only shown a modest reduction in nocturia[19] in patients with the best chance for benefit from such drugs ie. benign prostatic hypertrophy (BPH). Dizziness due to postural hypotension may limit the use of this class of drugs though tamsulosin (Flomax) and alfuzosin (Xatral) have the least hypotensive effect. There is no benefit using these drugs for nocturia in women.

5-Alpha-reductase inhibitors such as dutasteride (Avodart), finasteride (Proscar) reduce nocturia by decreasing the size of the prostate gland over four to six months. This group of drugs are only useful for men with BPH and may have added benefit in combination with an alpha-blocker.

Anticholinergics with antimuscarinic effects such as oxybutynin (Ditropan, Lyrinel XL), tolterodine (Detrusitol), solifenacin (Vesicare) reduce nocturia by having a bladder relaxant effect allowing an increase in bladder capacity and reduction in urge-associated void. They are more commonly prescribed to women than men due to concern about urinary retention. The most common side effects are dry mouth, constipation and urinary tract infection.

Inadequate night time levels of anti-diuretic hormone have been noted in patients with nocturia. Thus desmopressin (ddAVP Minirin) taken two hours prior to bedtime can reduce nocturnal polyuria and subsequent nocturia. This is available as a nasal spray and in tablet form though bioavailability is much better with the nasal spray. Patients with nocturnal polyuria who have normal bladder function can have a significant reduction in nocturia. Serum sodium levels need to be closely monitored given the risk of hyponatraemia which can be life threatening.

Desmopressin is not recommended for use in patients over 65 years of age, those with cardiac disease and patients who are on drugs, which can cause hyponatraemia (diuretics, nonsteroidal anti-inflammatory drugs, antidepressants, carbamazepine). Desmopressin has been shown to decrease nocturia significantly with improvement in sleep duration.[20]

Conclusion

Nocturia can be multifactorial and thus may require more than one strategy to help improve the condition. A multifaceted management plan is useful and will help address the various problems associated with nocturia and hopefully have a positive impact on quality of life, especially in the more vulnerable older age group.

Conflict of interest: none declared

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