

Management of Nocturia in men with lower urinary tract symptoms (LUTS)

Nocturia is defined as waking at night to void, specifically during the main sleep period (from falling asleep to the time of intending to rise).

It reflects the balance between nocturnal urine production and bladder storage capacity. Nocturia may be associated with lower urinary tract dysfunction (LUTD), including overactive bladder (OAB), chronic pelvic pain syndrome, and bladder outlet obstruction (BOO), though causality with BOO remains debated. **Importantly, nocturia can result from behavioural factors, sleep disturbances, or systemic conditions unrelated to LUTD.** Specifically, nocturnal polyuria, defined as a ratio of 40% or more of total 24 hr urine volume produced at night, is often linked to such extra-urolological diseases, such as sleep obstructive apnea.

Categories of nocturia

CATEGORY	Disproportionate urine production (at all times, or during sleep)	Low volume of each void (at all times, or overnight)
Behavioural	Inappropriate fluid intake	"Bladder awareness" due to secondary sleep disturbance
Systemic	Water, salt and metabolite output	
Sleep disorder	Variable water and salt output	"Bladder awareness" due to primary sleep disturbance
LUTD		Impaired storage function and increased filling sensation

Treatment of nocturia

1. Antidiuretic therapy

Desmopressin is a synthetic analogue of arginine vasopressin (AVP, the natural antidiuretic hormone) with selective V2 receptor activity and no relevant V1 effects. **It reduces nocturnal voids and improves sleep**, as shown in systematic reviews, without a significant increase in major adverse events.

Hyponatraemia is the key concern, particularly in older adults, requiring serum sodium monitoring before initiation, after dose titration, and during treatment.

Desmopressin oral disintegrating tablets (ODT) have demonstrated better outcomes than placebo, including greater reductions in nocturnal episodes and higher responder rates. However, clinically significant hyponatraemia was more frequent in patients aged ≥ 65 years, even at low doses.

Low-dose desmopressin ODT (50 mcg in men, 25 mcg in women) is approved in Europe, Canada, and Australia, and later in the United States by the Food and Drug Administration (FDA), with a boxed warning for hyponatraemia.

Desmopressin acetate nasal spray, a newer low-dose formulation with different bioavailability, has also shown statistically significant but modest benefit in randomised trials. Adverse event rates were low, and hyponatraemia occurred at a lower frequency. This formulation is FDA-approved but not available in Europe.

Practical considerations: a full medical evaluation is required to exclude non-urolological causes (e.g., sleep apnoea) before initiating desmopressin. In men < 65 years, treatment should start at a low dose and be titrated gradually. Patients should avoid fluid intake one hour before and eight hours after dosing. In older men, desmopressin should only be used if serum sodium is normal. Caution is advised in men > 75 years.

2. Medications to treat LUTD

In cases where nocturia is associated with LUTD, pharmacological treatments for storage or voiding symptoms may be considered.

These include selective $\alpha 1$ -adrenergic antagonists, antimuscarinics, 5-alpha-reductase inhibitors, and phosphodiesterase-5 inhibitors. However, the overall effect size for these treatments on nocturia is small or not significantly different from placebo.

Most available data on overactive bladder medications come from female-predominant populations, and no male-specific studies were identified. Combination therapies have shown inconsistent benefit.

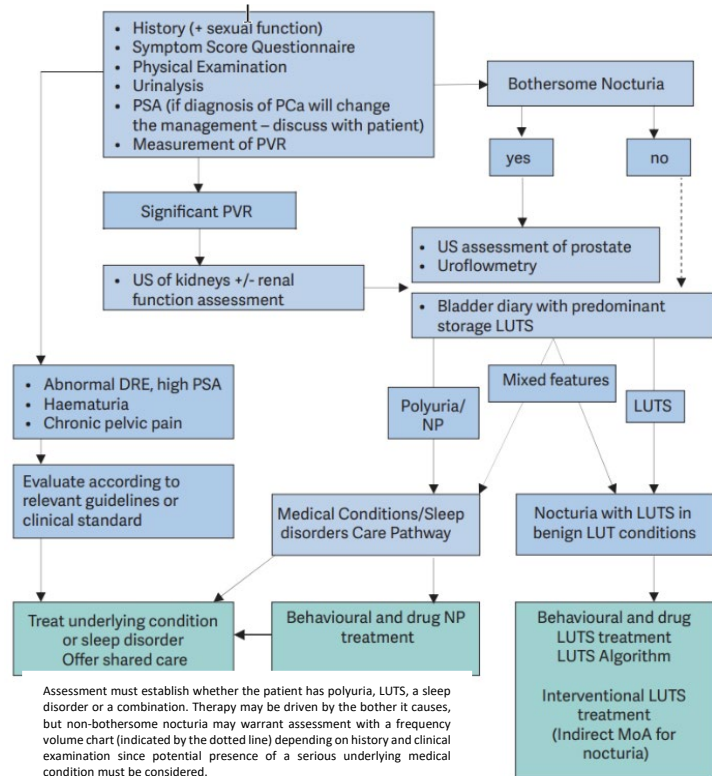
3. Other medications

Aetiologic treatment (such as treating sleep apnea) when present.

Additional pharmacological agents have been studied in relation to nocturia symptom response or quality-of-life improvement. These include **sleep-promoting agents, diuretics, non-steroidal anti-inflammatory drugs (NSAIDs), and phytotherapy**. The effect size of these agents is generally small or not significantly different from placebo. Some drugs have shown larger responses in individual studies, but larger confirmatory trials are lacking. Sleep agents may not reduce the number of nocturnal voids, they may help patients fall back asleep more easily.

Diagnostic assessment

Bladder diary is the cornerstone of evaluation of nocturia, especially when this symptom is isolated. Identifies key features such as bladder functional capacity, nocturia episodes number, and nocturnal polyuria if present.



Assessment must establish whether the patient has polyuria, LUTS, a sleep disorder or a combination. Therapy may be driven by the bother it causes, but non-bothersome nocturia may warrant assessment with a frequency volume chart (indicated by the dotted line) depending on history and clinical examination since potential presence of a serious underlying medical condition must be considered.

FVC = frequency volume chart; DRE = digital rectal examination; NP = nocturnal polyuria; MoA = mechanism of action; PVR = post-void residual; PSA = prostate-specific antigen; US = ultrasound.

■ Diagnosis ■ Treatment ■ Follow-up

Recommendations	Strength rating
Treat underlying causes of nocturia, including behavioural, systemic condition(s), sleep disorders, lower urinary tract dysfunction, or a combination of factors.	Weak
Discuss behavioural changes with the patient to reduce nocturnal urine volume and episodes of nocturia and improve sleep quality.	Weak
Offer desmopressin to decrease nocturia due to nocturnal polyuria in men < 65 years of age.	Weak
Offer low dose desmopressin for men > 65 years of age with nocturia at least twice per night due to nocturnal polyuria.	Weak
Screen for hyponatraemia at baseline, day three and day seven, one month after initiating therapy and periodically during treatment. Measure serum sodium more frequently in patients > 65 years of age and in patients at increased risk of hyponatraemia.	Strong
Discuss with the patient the potential clinical benefit relative to the associated risks from the use of desmopressin, especially in men > 65 years of age.	Strong
Offer $\alpha 1$ -adrenergic antagonists for treating nocturia in men who have nocturia associated with LUTS.	Weak
Offer antimuscarinic drugs for treating nocturia in men who have nocturia associated with overactive bladder.	Weak
Offer 5 α -reductase inhibitors for treating nocturia in men who have nocturia associated with LUTS and an enlarged prostate > 40 mL.	Weak
Do not offer phosphodiesterase type 5 inhibitors for the treatment of nocturia.	Weak