

**SIGNIFICANCE OF NOCTURIA IN DIURETIC TREATED PATIENTS: IMPACT ON SLEEP AND QUALITY OF LIFE****\*Sahla Ashraf, Dr. Lincy George, Emi Maria C. Baijo and Helga Rose**

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**ABSTRACT**

Nocturia, a common side effect of diuretic therapy, is often underlooked in hypertensive patients despite its significant impact on sleep and quality of life. Diuretics, while effective in reducing blood pressure and cardiovascular risk, increase urine output and can lead to nighttime awakenings, especially when administered later in the day. This review explores the association between diuretic use and nocturia, highlighting its underlying mechanisms, clinical implications, and consequences on sleep architecture and daytime functioning. It also discusses assessment tools and management strategies aimed at minimizing nocturia while preserving therapeutic efficacy. Recognizing and addressing diuretic-induced nocturia is crucial for optimizing both hypertension control as well as patient well-being.

**KEYWORDS:** Diuretics, Nocturia, Hypertension, Sleep disturbance, Quality of life, Quality of sleep.**1. INTRODUCTION**

Hypertension is considered one of the most prevalent chronic conditions around the world, with the majority of individuals relying on long-term pharmacotherapy to maintain their blood pressure under control. Within the spectrum of antihypertensive agents, diuretics, especially thiazides and loop diuretics, are widely regarded for their established efficacy, affordability, and their role in reducing cardiovascular risk. However, the mechanism of action of diuretics results in increased urine production, which can lead to an often-overlooked yet impactful side effect: nocturia.

Nocturia, waking up at night to urinate, is a widely reported symptom in the adult population, with a higher incidence among those diagnosed with hypertension. It significantly affects sleep patterns and can negatively influence the quality of life. Diuretics, widely prescribed to regulate high blood pressure, increase urine output and can contribute to nocturia, particularly when taken later in the day. Fragmented and disturbed sleep is frequently observed in patients suffering from nocturia, potentially causing daytime somnolence and adverse health outcomes. Therefore, it is essential to assess the extent to which nocturia affects sleep quality and health-related quality of life, and to examine the correlation between these factors.

This review explores the role of nocturia in patients receiving diuretic therapy for hypertension, focusing on

how it affects sleep quality and health-related quality of life (QoL).

**2. Understanding Nocturia**

Nocturia is a common urological symptom characterized by the need to wake from sleep, one or more times, during the night to urinate. According to the definition of the International Continence Society, nocturia is the complaint that an individual wakes one or more times to void urine at night. Diagnosis of nocturia is made when the patient wakes to urinate at night and each episode is followed by sleep, distinguishing it from insomnia or habitual waking. While it may appear benign, especially in its early stages, nocturia can significantly affect sleep continuity and overall quality of life, particularly when it occurs two or more times per night.

**2.1 Classification and Etiology**

Nocturia can arise due to a variety of underlying physiological or pathological processes. It is broadly classified into the following categories.

- **Nocturnal polyuria:** It is a condition in which the volume of urine voided during sleep exceeds 35% of the total 24-hour urine output. It can be associated with aging, congestive heart failure, obstructive sleep apnea, or medications like diuretics.
- **Nocturnal detrusor overactivity:** This condition is characterized by nocturia resulting from a diminished bladder capacity during sleep.

- **Mixed Nocturia:** It is characterized by a combination of nocturnal polyuria and limited bladder capacity.
- **Global Polyuria:** It is the condition in which the 24-hour urine production is above 2500cc. It may be due to conditions like diabetes mellitus, diabetes insipidus or excessive fluid intake.

## 2.2 Epidemiology and Risk factors

The prevalence of nocturia increases in frequency and severity with age, affecting over 50% of individuals over 60, with similar rates between men and women overall. However, younger women are more prone to experience nocturia than younger men, while in older adults the scenario is vice versa. Among men aged 70 to 79, about 50% experience two or more nightly voids. As the population ages, the prevalence of clinically significant nocturia is expected to rise further.

### Risk factors include

- Aging and decreased nocturnal secretion of antidiuretic hormone (ADH)
- Hypertension and diuretic use
- Sleep apnea and other sleep-related disorders
- Benign prostatic hyperplasia (BPH) in men and pelvic floor disorders in women
- Obesity
- Diabetes
- Renal disease
- Overactive bladder (OAB)
- Pregnancy, especially the third trimester.

## 2.3 Clinical Implications

According to the study conducted by Kim et.al., 2011 on the impact of nocturia on health-related quality of life suggested that nocturia has been recognized as a discrete clinical condition rather than a simple symptom. Recurrent nocturnal awakenings lead to poor sleep quality, fatigue, and daytime dysfunction. It is also linked to increased risks of depression, falls, and reduced productivity, mostly in elderly patients. In the context of hypertension management, nocturia can negatively impact treatment adherence, particularly if it is perceived as a medication-related side effect.

## 3. Diuretics in Hypertension Management

Diuretics have been recognized for a long time as an essential component in the management of hypertension. They act upon the tubules of nephron and work by promoting the excretion of sodium and water from the kidneys, thereby decreasing blood volume and peripheral vascular resistance. Diuretics are particularly appreciated for their efficacy, affordability, and proven ability to lower the risk of cardiovascular issues, including stroke and heart failure.

### 3.1 Types of Diuretics Used in Hypertension

Mainly three classes of diuretics are used in the treatment of hypertension, they are:

- **Thiazide diuretics (e.g., hydrochlorothiazide, chlorothiazide):** These are the most frequently prescribed diuretics and are among the WHO-recommended first-line treatments for hypertension. They work by blocking sodium reabsorption in the distal convoluted tubule.
- **Loop Diuretics (e.g., furosemide, torsemide):** More potent than thiazides, these drugs target the thick ascending limb of the loop of Henle. They are primarily used in patients with kidney dysfunction or fluid overload conditions.
- **Potassium-sparing Diuretics (e.g., spironolactone, eplerenone):** These agents reduce sodium reabsorption while preventing potassium loss. Spironolactone, in particular, is effective in resistant hypertension due to its ability to block aldosterone receptors.

### 3.2 Mechanism of Action and its Antihypertensive Effect

Diuretics are class of drugs used in the management and treatment of edematous and other non-edematous disease conditions. These are substances that increase the production and volume of urine by suppressing receptors that facilitate the reabsorption of Na<sup>+</sup>, the most abundant extracellular cation, from the renal tubules, thereby increasing the osmolality of the renal tubules and thus suppressing water reabsorption. They also reduce extracellular fluid volume by increasing urinary sodium and water excretion. This results in a reduction in plasma volume, cardiac output, and eventually peripheral vascular resistance.

Different classes of diuretics act at specific sites in the nephron: thiazide diuretics inhibit sodium-chloride reabsorption in the distal convoluted tubule; loop diuretics block the sodium-potassium-chloride transporter in the thick ascending limb of the loop of Henle, leading to more potent fluid loss; and potassium-sparing diuretics work in the collecting ducts, either by antagonizing aldosterone (e.g., spironolactone) or blocking sodium channels (e.g., amiloride).

Diuretics help lower blood pressure primarily by reducing circulating blood volume. The initial drop in blood pressure results from a decrease in plasma volume and cardiac output. Over time, compensatory mechanisms such as vascular resistance may increase, but diuretics also exert long-term effects by reducing sodium content in the arterial wall and improving vessel compliance, leading to sustained reductions in peripheral vascular resistance.

## 4. Diuretics induced Nocturia

Diuretics, including thiazide and loop diuretics, promote the excretion of sodium and water and are commonly used in the management of hypertension. As a result, urine production increases markedly for several hours after dosing. The effect of diuretics can persist for several hours following administration. When taken later

in the day, this effect continues into the night, leading to episodes of nocturnal urination and hence resulting in sleep disruptions. This side effect is especially relevant for elderly patients or those with already reduced bladder capacity.

#### 4.1 Mechanism of diuretics induced nocturia

Diuretics act on various segments of the nephron to increase the excretion of sodium and water. This natriuretic and diuretic effect leads to increased urine output (diuresis), which is beneficial for reducing plasma volume and lowering blood pressure. However, when the timing or pharmacokinetics of these medications overlap with the patient's sleep period, it results in nocturnal diuresis.

- **Thiazide diuretics**, which have a moderate and sustained action, may still exert effects into the evening if taken late in the day.
- **Loop diuretics**, such as furosemide, have a more potent but shorter duration of action. If dosed later in the day, their peak effect may coincide with sleep hours, increasing nighttime urination.
- **Potassium-sparing diuretics**, like spironolactone, tend to have a longer half-life and are less commonly associated with acute diuresis, but their use in combination therapy can contribute cumulatively to nocturnal symptoms. Nocturia due to diuretics is pharmacologically predictable, particularly when the timing of administration does not allow for full diuretic clearance before sleep. Since urine output typically peaks within 1–4 hours after administration, late dosing shifts this peak into the sleep window.

### 5. Nocturia and Sleep Disturbance

Quality sleep is essential for physical, emotional, and cognitive wellbeing. Nocturia interrupts sleep continuity by producing frequent awakenings throughout the night. This sleep fragmentation reduces sleep efficiency, which can result in excessive daytime drowsiness mood disturbances, and poor daily functioning.

As nocturia frequency increases, patients experience more sleep-related problems, such as difficulties falling asleep, feeling unrefreshed when they wake up, and greater daytime tiredness. These interruptions contribute to a vicious cycle of poor sleep and worsening health, emphasizing the importance of clinicians addressing sleep abnormalities in patients on diuretic therapy.

#### 5.1 Disruption of Sleep Architecture

Sleep takes place in cycles consisting of non-REM and REM phases. Both REM and deep sleep, also known as slow-wave sleep, are necessary for both mental and physical recovery. These cycles are disrupted by nocturia, which frequently leads to shorter deep and REM sleep durations, fragmented sleep, higher sleep latency (time taken to fall back asleep), and decreased overall sleep time.

#### 5.2 Assessment Tools for Sleep Quality

- **Pittsburgh Sleep Quality Index (PSQI)**: a self-report questionnaire that assesses sleep quality over a one-month time interval. It assesses overall sleep quality by evaluating seven key domains: subjective sleep quality, sleep latency, sleep duration, habitual sleep efficiency, sleep disturbances, use of sleeping medication, and daytime dysfunction
- **Actigraphy**: It is a non-invasive wearable device that tracks sleep-wake patterns.
- **Sleep Diaries**: Patient-maintained records of bedtime, wake time, nocturnal awakenings, and perceived quality of sleep.

#### 5.3 Daytime Consequences of Sleep Disturbance

Chronic sleep interruption due to nocturia leads to significant daytime dysfunction including.

- Excessive daytime fatigue with diminished vigilance.
- Emotional dysregulation, including increased irritability, anxiety symptoms, and depressive mood.
- Neurocognitive dysfunction, particularly working memory deficits and impaired sustained attention.
- Functional decline in occupational productivity and social participation.
- Increased risk of falls and fractures in geriatric populations.

### 6. Impact of Nocturia on Quality of Life (QoL)

Nocturia, particularly when induced by diuretic therapy in hypertensive patients, extends its impact beyond sleep disruption to affect overall quality of life (QOL). It has been associated with reduced physical, emotional, and social well-being. The repeated interruption of sleep can contribute to emotional instability, irritability, and even depression. Cognitive dysfunction such as poor concentration and memory issues are also linked to this. The abnormal sleep patterns result in sleep deprivation and daytime sleepiness leading to persistent fatigue and reduction in activity levels. In patients with hypertension, this disturbance is particularly concerning, as poor sleep is independently associated with increased cardiovascular risk, impaired blood pressure control, and reduced treatment adherence.

Furthermore, nocturia has been associated with social withdrawal and decreased confidence probably due to exhaustion from interrupted sleep.

In a nutshell, nocturia has a negative impact on overall quality of life. Increased nocturia is associated with lower QOL scores and greater perceived symptom burden. For individuals managing a chronic condition like hypertension these symptoms not only affect their personal and social lives but also hinder them from adhering to their medications.

#### 6.1 QoL Measurement Tools

- **EQ-5D**: Measures five dimensions of health. A widely tool which assesses five dimensions of

health—mobility, self-care, usual activities, pain/discomfort, and anxiety/depression

- **EQ-VAS (Visual Analogue Scale):** It is a self-rated measure of overall health, which tends to decline in individuals experiencing chronic sleep loss.
- **N-QoL (Nocturia-Quality of Life):** Focuses on nocturia-specific QoL effects, highlighting the emotional and lifestyle impacts of nighttime voiding.

## 7. Clinical Implication and Management Strategies

### 7.1 Timing of Diuretic Administration

The timing of diuretic administration is one of the most modifiable factors influencing the occurrence of nocturia. Morning dosing is generally recommended to minimize the likelihood of nocturnal diuresis. Administering diuretics earlier in the day ensures that peak diuretic activity diminishes by bedtime, thereby reducing the chances of nighttime awakenings.

In patients requiring a twice-daily regimen, the second dose should ideally be administered by early evening to allow for adequate diuresis during waking hours. This timing can help maintain blood pressure control while minimizing disruptions to sleep.

### 7.2 Dose Adjustment and Drug Selection

Tailoring diuretic therapy is crucial for managing bothersome nocturia.

- **Dose minimization:** Reducing the dose to the lowest effective amount can decrease nocturnal urination.
- **Alternative agents:** Substituting or supplementing with non-diuretic antihypertensives (e.g., ACE inhibitors, ARBs, or calcium channel blockers) may be appropriate in patients at low cardiovascular risk or those experiencing intolerable sleep disturbances.
- **Drug selection:** Choosing long-acting thiazide-like diuretics (e.g., chlorthalidone) may be beneficial for some patients but requires caution due to prolonged action extending into nighttime.

### 7.3 Combination Therapy

Combining diuretics with other antihypertensive agents may allow for lower diuretic doses, reducing the risk of nocturia while maintaining blood pressure control. Diuretic-sparing combinations may also be considered in patients with well-controlled BP and significant sleep issues.

### 7.4 Non-pharmacological Approach

Lifestyle adjustments can complement pharmacologic strategies.

- Limiting evening fluid intake, particularly after 6 p.m.
- Reducing caffeine and alcohol consumption, which can irritate the bladder and increase urine production.
- Managing comorbidities such as sleep apnea, diabetes, or prostate enlargement.

- Bathing routines are being recognized to help reduce nocturia, especially taking warm water baths.
- Encouraging healthy sleep hygiene (consistent sleep schedule, reduced screen time) may further help improve sleep resilience.

### 7.5 Patient Education and Monitoring

Educating patients on the relationship between diuretic timing and nocturia empowers them to involve in their disease management and increase their medication adherence. Clinicians should.

- Inquire about sleep disturbances at each visit.
- Reinforce the importance of adherence to morning dosing.
- Adjust therapy based on individual symptom burden and using tools such as the PSQI or nocturia frequency diaries.

By integrating patient-reported outcomes and shared decision-making, clinicians can maintain optimal blood pressure control while reducing the impact of nocturia.

### 7. Multifactorial Nature of Nocturia in the Elderly

While diuretic therapy is a known contributor to nocturia, the condition is often multifactorial—particularly in elderly patients. Physiological changes such as decreased bladder capacity, impaired kidney function, and altered circadian rhythm of urine production play a role. Comorbidities like diabetes, heart failure, and sleep apnea can further exacerbate nocturnal urination. Other contributing factors include.

- Late evening fluid intake
- Alcohol use
- Sedative medications
- Calcium supplements

Comprehensive clinical assessments, including drug reviews and management of comorbidities, are necessary for effective treatment.

## 8. CONCLUSION

Nocturia is a common and often overlooked side effect of diuretic therapy in the management of hypertension. While diuretics remain essential for blood pressure control and cardiovascular risk reduction, their tendency to cause nocturnal urination can significantly impair sleep quality and, in turn, reduce overall quality of life—particularly in older adults and those with comorbid conditions.

The physiological basis of diuretic-induced nocturia is well understood, and clinical evidence consistently links it to sleep fragmentation, daytime dysfunction, and emotional distress. These consequences can negatively affect treatment adherence and long-term blood pressure outcomes, making nocturia an important factor in comprehensive hypertension care.

Through evidence-based strategies, including optimal dosing schedules, personalized pharmacotherapy, and patient education, healthcare providers can reduce



nocturia-related sleep disturbances and improve adherence. Incorporating validated assessment tools like the PSQI and EQ-5D can enhance patient monitoring and optimize clinical outcomes.

Ultimately, a patient-centered, multidisciplinary approach is essential to balance blood pressure control with quality of life in individuals affected by nocturia.

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