What is the significance of Nocturnal polyuria in Nocturia?

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Nocturia is a significantly underestimated medical problem that seriously affects patients' quality of life, work engagement, productivity, and well-being. It is a common condition, proven to be the most bothersome for patients with Lower Urinary Tract Symptoms [1]. It is well known that two or more nocturnal voids are the clinically meaningful threshold associated with significant adverse consequences to health and well-being [2]. Commonly associated consequences include increased mortality and morbidity, increased risk of falls and hip fractures, traffic and work accidents, increased risk of cardiovascular diseases, and diabetes mellitus [2]. Additionally, interrupted sleep patterns can contribute to mood disturbances, such as irritability and depression [2]. It also provokes immunological problems and dysfunction of memory and perception, daytime fatigue, decreased productivity and work performance, and impaired cognitive function. Overall deteriorates the quality of life and increases health costs [2,3].

Hence, the importance of taking sleep into account should be emphasized when assessing the relationship between nocturia and associated outcomes [3]. It is worth mentioning that nocturia is just as prevalent in women as in men, especially in postmenopausal women [4,5].

Regarding pathophysiology, the main causes that provoke nocturia are nocturnal polyuria, global polyuria, urinary bladder dysfunction, sleep disorders, and circadian clock disorders. Urinary bladder dysfunction includes reduced bladder capacity, detrusor overactivity, and other mixed etiologies [6].

Nocturnal polyuria is a medical condition characterized by excessive urine production during the night, leading to disrupted sleep patterns and frequent nighttime bathroom visits. Despite its prevalence, this condition is frequently undiagnosed or overlooked, resulting in considerable discomfort and a diminished overall quality of life for affected individuals. Two definitions of nocturnal polyuria exist. The classical and widely adopted definition considers nocturnal polyuria as nocturnal urine production above 20% for young patients and 33% for older patients (>65y) [2]. The other definition defines nocturnal polyuria as nocturnal urine production of >90 ml/h during night sleep [5].

Nocturnal polyuria is more common than one might think, particularly among the elderly. However, due to its often-subtle symptoms and limited awareness, many cases go undiagnosed or misdiagnosed as other conditions, such as overactive bladder or urinary tract infections. Nocturnal polyuria seems to be the most common cause of nocturia. According to the prevailing definition [7], the prevalence of nocturnal polyuria, in both genders, is 44% in those under 65 years, and 31.3% in those 65 years or older [8]. In a recent study, 31.5% of men and 38,5 of women had nocturnal polyuria when the classical definition was used and 23.8% and 18.1% of men and women respectively presented nocturnal polyuria under the nocturnal urine production definition [9]. It seems that more research and evidence are needed to reach a consensus about the most accurate definition for use in everyday clinical practice [10].

Numerous factors can contribute to the development of nocturnal polyuria. Several non-urological causes are known to provoke this dysfunction. Such causes are untreated diabetes mellitus or insipidus,

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sleep disorders because of obstructive sleep apnea, cardiovascular diseases (hypertension, heart failure) [11], chronic kidney disease, certain medications, varicose veins of the lower extremities, and primary polydipsia. Identifying and addressing these risk factors appropriately is pivotal in effectively managing and treating nocturnal polyuria. If there is not any obvious disorder provoking nocturnal polyuria, the condition is classified as nocturnal polyuria syndrome [12,13]. The interplay among nocturnal polyuria and pathological conditions such as hypertension, arteriopathy and arterial stiffness, coronary heart disease, and distribution in the third space of body fluid is deemed significant and the focus of current research [13]. This is also observed in the context of the role of brain natriuretic peptide [13].

Nocturnal polyuria leading to nocturia, with a constant need to wake up and urinate that disrupts sleep and yields consequential outcomes. The coexistence of nocturia resulting from urological conditions, such as overactive bladder and bladder outlet obstruction and nocturnal polyuria aggravates the whole clinical condition.

The diagnosis of nocturnal polyuria involves a thorough assessment of an individual's medical history, physical examination, and specialized tests, such as urine volume measurement and frequency charts. Notably, in the case of nocturnal polyuria, a frequency-volume chart serves as the cornerstone for the diagnosis of this condition [14].

Following diagnosis, diverse treatment options are available, including lifestyle modifications, behavioral therapies, and pharmacotherapy. It is essential for healthcare professionals to be knowledgeable about these options and work closely with patients to develop personalized treatment plans [6].

The treatment rationale for nocturia underscores that nocturnal polyuria, attributed to inadequate antidiuresis, is a major contributing factor to nocturia. Before starting any pharmaceutical treatment, it would be beneficial to try some lifestyle modifications, as these can offer an improvement of nocturnal polyuria. For instance, reducing caffeine, alcohol, and generally fluid intake a couple of hours before bedtime, could be of benefit to the patient [14]. Furthermore, the administration of desmopressin offers a significant reduction in nocturia episodes and nocturnal urine production, leading to improvements in sleep and quality of life [15-18]. Contemporary formulations of desmopressin are well-tolerated, with a relatively low risk of hyponatremia with appropriate dosing escalation. A lower minimum effective dose in females is needed compared to males [18-20]. Furthermore, sodium monitoring just before treatment initiation and on the first, third, and seventh days of treatment is essential. Research for the treatment of nocturnal polyuria is ongoing and includes highly selective arginine vasopressin 2 receptor agonists, non-steroid anti-inflammatory drugs, sex hormone replacement treatment, and short-acting diuretics [18].

Raising awareness about nocturnal polyuria is crucial to ensure timely diagnosis and effective management. Individuals grappling with frequent nighttime urination should refrain from dismissing it as a routine aspect of aging or underestimating its impact on their well-being. Initiating a dialogue with healthcare providers, and openly discussing symptoms, can pave the way for early intervention and subsequently enhance overall quality of life.

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