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Nocturia in Adults: Etiology and Classification

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Nocturia is one of the most bothersome of all urologic symptoms, yet even a rudimentary classification does not exist. We herein propose a classification system of nocturia based on a retrospective study. The records of 200 consecutive patients with nocturia were reviewed. Evaluation included history, micturition diary (including day, night, and 24-hr voided volume), postvoid residual urine (PVR), and videourodynamic study (VUDS). Functional bladder capacity (FBC) was determined to be the largest voided volume in a 24-hr period. The etiology of nocturia was thus classified into one of three groups: nocturnal polyuria ([NP] in which voided urine volume during the hours of sleep exceeds 35% of the 24-hr output), nocturnal detrusor overactivity ([NDO] defined as nocturia attributable to diminished bladder capacity during the hours of sleep), and mixed (NP + NDO); polyuria (24-hr urine output >2,500 cc) was classified separately.

There were 129 women and 65 men ranging in age from 17 to 94 years (x = 59). Overall 13 (7%) had NP, 111 (57%) NDO, and 70 (36%) had a mixed etiology of their nocturia (both NP and NDO). Forty-five (23%) also had polyuria. These data confirm that the etiology of nocturia is multifactorial and in many instances unrelated to the underlying urologic condition. Nocturnal overproduction of urine is a significant component of nocturia in 43% of patients, most of whom will also have NDO. We believe that treatment should be directed at both conditions. *Neurourol. Urodynam. 17:467–472, 1998.*

Key words: nocturia; classification system

INTRODUCTION

Although appropriate treatment of nocturia depends on recognition of its pertinent pathogenic mechanisms, the etiology remains unclear in a significant proportion of patients. Indeed, difficulty in assessing the cause of nocturia may explain why surgical therapy is more than occasionally ineffective [Matthiesen et al., 1996; Sullivan and Yalla, 1993]. We herein propose a system for classification of nocturia based on a retrospective analysis of voiding diaries in patients with the symptom for the purpose of improving accuracy of its treatment.

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TABLE I. Voiding Diary Analysis

	Males (n = 65)	Females (n = 129)	BPH (n = 15)	UI (n = 8)	SUI (n = 25)	DI (n = 52)
NP (n = 13)	5% (3)	8% (10)	0% (0)	25% (2)	16% (4)	13% (7)
NDO (n = 111)	48% (31)	62% (80)	33% (5)	25% (2)	56% (14)	54% (28)
Mixed (n = 70)	48% (31)	30% (39)	67% (10)	50% (4)	28% (7)	33% (17)
NP/Mxd (n = 83)	52% (34)	38% (49)	67% (10)	75% (6)	44% (11)	46% (24)
Poly (n = 45)	34% (22)	18% (23)	27% (4)	13% (1)	8% (2)	14% (7)

METHODS

The records of 200 consecutively selected patients complaining of nocturia as part of their voiding symptom complex were reviewed (six patients being excluded due to lack of voiding diaries) and the following data tabulated: 1) postvoid residual urine (PVR); 2) day, night (regardless of the number of hours of sleep; patients did not specify the number of sleep hours); and 24-hr voided volumes; 3) clinical diagnosis; 4) urodynamic diagnosis. Evaluation included history, micturition diary, PVR, and videourodynamic study (VUDS). Functional bladder capacity (FBC) was taken to be the largest single void in a typical 24-hr period [Abrams et al., 1988]. Nocturnal polyuria (NP) was defined as overnight urine volume (NUV) >35% of the 24-hr total urine volume [Rollema, 1994]. Polyuria was defined as a 24-hour urine output >2,500 cc [Griffiths et al., 1993; Saito et al., 1993]. The ratio NUV/FBC was defined as the Nocturia Index (NI), significant in that this ratio defines how many times a person would be predicted to arise to void based on a comparison of bladder capacity and nocturnal urine output volume. Specifically, NI-1 = predicted nightly voids (PNV). In accordance with these data, the etiology of nocturia was classified into one of three groups: pure NP, nocturnal detrusor overactivity (NDO), and mixed (NP + NDO). Patients in the mixed group are not included in the NP or NDO groups; the three are mutually exclusive. Patients with polyuria were classified separately but may overlap with the aforementioned three nocturia categories.

We additionally examined the correlation between categories of nocturia and several clinical/urodynamic diagnoses. Diagnostic categories included males, females, benign prostatic hypertrophy (BPH), urge incontinence (UI), stress urinary incontinence (SUI), and detrusor instability (DI). A comparison group called None was defined as patients without BPH, UI, SUI, and DI. Comparison was made of the population of patients having both pure NP and mixed etiologies of nocturia (NP/mixed), and those having nocturia owing to pure NDO. Statistical analysis was carried out using Fisher's Exact Test and Odds Ratios [Fleiss, 1981].

RESULTS

There were 129 women (66%) and 65 (34%) men ranging in age from 17 to 94 years (mean, 59 years). Of these, 15 (23% of men) had BPH, eight (4%) had UI, 25 (13%) had SUI, and 52 (27%) had DI. These four clinical categories were not mutually exclusive. Overall 13 (7%) had NP, 111 (57%) NDO, and 70 (36%) had a mixed etiology of their nocturia (both NP and NDO). Forty-five (23%) also had polyuria. The 194 patients studied were divided into five groups (see Table I).

TABLE II. Estimates and 95% Confidence Intervals (Males vs. Females)

	Estimate (%/no.)	95% C.I. lower bound (%)	95% C.I. upper bound (%)
Males			
NP	5% (3/65)	2	14
NDO	48% (31/65)	37	60
Mixed	48% (31/65)	37	60
NP/mixed	52% (34/65)	41	65
Polyuria	34% (22/65)	24	47
Females			
NP	8% (10/129)	5	14
NDO	62% (80/129)	54	70
Mixed	30% (39/129)	23	39
NP/mixed	38% (49/129)	30	47
Polyuria	18% (23/129)	13	26

1. NP: 13 patients (7%).
2. NDO: 111 patients (57%).
3. Mixed nocturia: 70 patients (36%) with both NP and NDO.
4. NP/Mixed: 83 patients (43%) with both pure NP (first group) or mixed (third group), this group having NP as at least a component of the etiology of their nocturia. This is referred to below as the NP/mixed group.
5. Polyuria: 45 patients (23%) with polyuria.

Table II provides estimates and 95% confidence intervals for each patient subgroup in males versus females [Fleiss, 1981].

The data display a trend such that males presenting with nocturia are more likely to have NP/mixed and less likely to have NDO compared to females presenting with nocturia (Fisher's Exact Test $P = 0.00$). Moreover, there is a statistically significant difference in the rates of NP, NDO, and mixed for the subgroups BPH, UI, SUI, DI, and none of the above (Fisher's Exact Test $P = 0.0005$).

Another way to describe the data is that among patients presenting with nocturia, the odds of a male having NP/mixed rather than NDO is 1.79 times higher than the odds of a female having NP/mixed rather than NDO (i.e., odds ratio (OR) = 1.79, $P = 0.057$). Note, the *P*-value for an OR is the probability that the odds of having NP/mixed are the same for males and females given the data. Patients with BPH and urge incontinence are significantly more likely to have NP/mixed compared to those patients without any of the problems listed (OR = 3.88, $P = 0.016$ and OR = 5.81, $P = 0.029$, respectively). The comparison group None is the group of patients without BPH, UI, SUI, and DI; among these patients, 32 of 94 (34%) had NP/mixed and 62 of 94 (66%) had NDO.

The chance of men having polyuria is significantly higher compared to women (OR = 2.36, $P = 0.013$). The rates of polyuria are also statistically different among all but one of the diagnostic subgroups (excluding the group with SUI) (Fisher's Exact Test $P = 0.023$). Patients with SUI and DI have significantly lower odds of having polyuria than patients without any of the listed diagnostic characteristics. Again, patients without BPH, UI, SI, and DI is the None comparison group; 31of 94 (33%) of these patients have polyuria. Table III gives the OR for NP/mixed and polyuria for the various subgroups.

TABLE III. OR and Associated *P*-Values

	OR	2-sided *P*-value
NP/mixed (vs. NDO)		
Males vs. females	1.79	0.057
BPH vs. None*	3.88	0.016
UI vs. None	5.81	0.029
SUI vs. None	1.52	0.48
DI vs. None	1.66	0.15
Polyuria (vs. Not)		
Males vs. females	2.36	0.013
BPH vs. None	0.74	0.77
UI vs. None	0.29	0.28
SUI vs. None	0.18	0.022
DI vs. None	0.32	0.010

*None is the group without BPH, UI, SUI, and DI.

DISCUSSION

To our knowledge, categories of nocturia and their potential implications as to etiology have not been studied in detail. Regardless of cause, >72% of elderly adults arise at least once a night with the urge to void and 24% routinely arise three or more times [Barker and Mitteness, 1988; Sommer et al., 1990]. With regard to the bothersomeness of nocturia, it has been found that 55% of women age 40–60 years complain of nocturia. Of these, 75% are mildly, 21% moderately, and 4% greatly bothered with that symptom. In addition, 95% of women with nocturia arise once or twice: 22% of these consider it a problem; it is a serious problem for 2%. The remaining 5% women arise more than twice to void: Of these, 83% consider nocturia a problem; it is considered a serious problem for 37% [G. Lose, personal communication].

Nocturia refers both to the simple notion of urinating during the night and to the more complex idea involving an excess of some sort. It is unclear whether the excess refers to the volume of urine being produced or being voided or to the number of occasions on which urine is passed. What constitutes an excessive frequency or volume for nocturnal urination seems not to have been formalized for any age group and certainly not for the elderly [Shah, 1989; Hennessy and Shen, 1986]. In this study, the term nocturia refers simply to the voiding of urine during the night. No assessment is made of whether such urination is excessive [Barker and Mitteness, 1988].

We herein define a ratio designated as the Nocturia Index, equal to NUV/FBC. An example of its utility is as follows: if one's FBC is 500 cc and 1,000 cc of urine is manufactured during the hours of sleep (NUV = 1,000), 500 cc would be voided during h.s. and the remainder eliminated with the first morning void (predicted nocturia ×1). Thus, in this illustration, NUV/FBC − 1 = 1, the PNV. A measure of NDO was defined as the difference between actual number of nightly voids (ANV) and PNV: The NDO index is thus ANV − PNV, a number reflecting the degree to which nightly bladder capacity differs from the maximum or FBC. Patients were described as having NDO if the NDO index was a number greater than zero (detailed derivations of NDO indices are not presented here). In other words, NDO exists when patients arise to void more frequently than predicted based on information derived from the voiding diary.

A common cause for patient visits to urologists [Barry et al., 1992], nocturia causes fatigue due to sleep deprivation and increases chances for traumatic injury from falls by the elderly [Barker and Mitteness, 1988]. Pathogenic factors for nocturia include cardiovascular disease, diabetes mellitus and insipidus, lower urinary tract obstruction, and awakening to void for other reasons [Matthiesen et al., 1996; Saito et al., 1993; Barker and Mitteness, 1988; Asplund and Aberg, 1992]. Behavioral and environmental factors contributing to nocturia include consumption of diuretic medication, caffeine, alcohol, or excessive fluid shortly before retiring [Barker and Mitteness, 1988]. Prostatic disease, urethritis, and neurogenic and unstable bladders have been reported to lead to frequent nocturnal rising [Saito et al., 1993; Barker and Mitteness, 1988]. Nocturia may additionally result from diabetes, stroke, congestive heart failure, peripheral edema, and myeloneuropathy secondary to vertebral disc disease or spondylosis [Sullivan and Yalla, 1993].

Nocturia in a large proportion of elderly men with lower urinary tract symptoms is caused by NP and natriuresis [Matthiesen et al., 1996]. Interestingly, a positive correlation has been observed between NUV and daytime mean arterial blood pressure. Although significant negative correlation has been found between NUV and plasma angiotensin II, NP is associated with decreased plasma vasopressin levels [Matthiesen et al., 1996]. A possible explanation for NP and natriuresis in these patients is that pressure-induced lesions in the renal medulla and distal tubular system may be occasioned by long-lasting urinary tract obstruction. This may interfere with normal circadian renal handling of sodium by decreasing diurnal sodium excretion [Matthiesen et al., 1996].

An increase in urine volume during sleep may be induced by three physiological changes related to aging: 1) The circadian rhythm of antidiuretic hormone and the renin-angiotensin-aldosterone system may be abnormal. 2) There are changes in glomerular filtration rate or renal plasma flow in association with a reduced distal tubular concentrating ability. 3) An impaired cardiovascular system may not supply a sufficient amount of blood to the kidneys during waking hours [Saito et al., 1993].

In our study, men, especially those with BPH, were more likely to have both NP and polyuria as a cause for nocturia than were women. Paradoxically, patients presenting with UI are more likely to have NP than those lacking a diagnosis of UI. Clearly then, treatment of nocturia should be based on its specific cause, rather than related but possibly irrelevant established urologic diagnoses. Since so many patients in our study had NP as a component of their nocturia, this disorder of circadian variation in urine output needs be addressed. Options for treatment of NP include evening fluid restriction (a form of behavior modification), timed diuretics, afternoon naps, morning application of compressive stockings when appropriate, and vasopressin administration [Saito et al., 1993; Sommer et al., 1990; Griffiths et al., 1992; Asplund, 1995; Donahue and Lowenthal, 1997].

CONCLUSIONS

We found that nocturnal overproduction of urine is a significant component of nocturia in 43% of patients. Our data confirm that the etiology of nocturia is multifactorial and often unrelated to the underlying urologic condition. It is concluded that many patients, even those with proven BPH or DI, may benefit from treatment directed at NP.

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