

Evaluation of the Etiology of Nocturia in Men: The Nocturia and Nocturnal Bladder Capacity Indices

Jeffrey P. Weiss,* Jerry G. Blaivas, Doron S. Stember, and David C. Chaikin

Weill Medical College of Cornell University, The New York Presbyterian Hospital, New York, New York

To determine and quantify the cause of nocturia in men, we describe and evaluate the relative contribution of two complementary indices of nocturia: the nocturia index (Ni), a measure of nocturnal urine overproduction, and the nocturnal bladder capacity index (NBCi), reflective of nocturnal bladder capacity. The records of 100 consecutive men with lower urinary tract symptoms (LUTS), having undergone video-urodynamic studies (VUDS), were prospectively studied. Evaluation included American Urological Association symptom score (AUASS), micturition diary (day, night, and 24-hr voided volume), and VUDS. Voiding diary analysis was carried out as previously described by us, determining the Ni, NBCi, and nocturnal polyuria index (NPi) (nocturnal urine volume/24-hr urine volume). In the case of AUASS question #7 (degree of nocturia), the odds of having a severe AUA question #7 response was found to be 4.09 times higher for patients with NBCi >2.0 compared with patients whose NBCi was \leq 2.0 using logistic regression analysis. In comparing patients with severe nocturia and low NBCi with those having mild nocturia and low NBCi, Ni performed in a fashion superior to NPi in identifying relative nocturnal urine overproduction as the suspected explanation for their nocturia (Ni = 3.42 vs. 1.42, $P = 0.0002$ cf. Npi = 0.44 vs. 0.27, $P = 0.018$, Mann-Whitney test, respectively). We suggest a discriminating threshold of NBCi >2 as highly significant in defining diminished NBC as a factor in the etiology of nocturia. In addition, we propose Ni of 1.5 as a threshold greater than which nocturia may be attributed to nocturnal urine overproduction in excess of maximum bladder capacity. Together, these indices describe in quantitative fashion the relative contributions of nocturnal urine overproduction and diminished NBC in identifying the etiology of nocturia in male patients. *NeuroUrol. Urodynam.* 18:559–565, 1999.

© 1999 Wiley-Liss, Inc.

Key words: nocturia; indices; etiology

INTRODUCTION

Nocturia may be attributed to increased nocturnal urine output (nocturnal polyuria [NP]), diminished nocturnal bladder capacity (NBC), or a combination of the two. Until now, parameters useful for quantification of these various etiologies have been lacking. We describe and evaluate two complementary indices of nocturia, the

*Correspondence to: Jeffrey P. Weiss, M.D., 400 E. 56th Street, New York, NY 10022. E-mail: Urojock@aol.com

Received 21 October 1998; Accepted 14 May 1999

© 1999 Wiley-Liss, Inc.

TABLE I. Definitions in Lexicon of Classification and Etiology of Nocturia

NUV (nocturnal urine volume):	Nightly voided volume plus first morning voided volume
FBC (functional bladder capacity):	Largest single recorded voided volume from 24-h diary
Nocturia index (Ni):	NUV/FBC
ANV (actual number nightly voids):	Recorded from diary
PNV (predicted number nightly voids):	Ni - 1
Nocturnal bladder capacity index (NBCi):	ANV - PNV
Nocturnal polyuria index (NPi):	NUV/24-h total voided volume

nocturia index (Ni), a measure of nocturnal urine overproduction relative to functional bladder capacity (FBC), and the NBC index (NBCi), reflective of NBC. Together, these indices describe in quantitative fashion the relative contributions of nocturnal urine overproduction and diminished NBC in the cause of nocturia in male patients.

MATERIALS AND METHODS

The records of 100 consecutive neurologically normal men with lower urinary tract symptoms (LUTS) having undergone video-urodynamic studies (VUDS) were prospectively studied. Evaluation included American Urological Association symptom score (AUASS), micturition diary (day, night, and 24-hr voided volume), and VUDS. Voiding diary analysis was carried out as previously described by us [Weiss et al., 1998], determining the Ni, NBCi, and NP index (NPi). Ni is defined as nocturnal urine volume (NUV) divided by FBC (the largest single voided volume from a 24-hr diary): If Ni is >1 , nocturia occurs owing to nocturnal urine output in excess of the bladder's maximal storage capacity. An Ni of >1 may be due to increased nocturnal urine production (NP), reduced NBC, or both. NP is defined as an NPi (NUV/24-hr urine output) $>35\%$ [Rollema, 1994].

The NBCi is a parameter derived as follows: Ni - 1 is the predicted number of nightly voids (PNV). This parameter assumes that NBC is maximal. The extent to which this is not the case (e.g., when NBC is less than maximal) is described by the difference between actual number of nightly voids (ANV) and PNV. This difference is known as the NBCi (formerly known as the NDOi [Weiss et al., 1998]). The greater the NBCi, the less the bladder capacity during sleep hours. We replaced the term NDOi with NBCi so as not to imply a urodynamic diagnosis of detrusor instability in nocturic patients. ANV recorded by diary (ANV) was subcategorized as mild (nocturia ≤ 2) versus severe (nocturia ≥ 3). A similar dichotomous analysis was applied to question #7 of the AUASS; responses to AUA #7 and voiding diary quantification of ANV were compared. The Ni, NBCi, and NPi were correlated for each diary-based nocturia severity subcategory. Comparisons were then made between the three combinations of high or low NBCi plus mild or severe nocturia, and the NBC, Ni, and NPi. Table I provides a summary of the nomenclature used in the lexicon of classification of nocturia.

RESULTS

There were 87 men with diary and VUDS data satisfactory for analysis. Overall 48 had mild and 39 had severe AUASS responses. Mean age was 68 and 65 years for mild and severe groups, respectively. Forty-five men had diary data satisfactory for

TABLE II. Summary of Correlations Between Nocturia Indices and Combinations of Nocturia Severity Categories

Nocturia severity category	NBCi (avg)	Ni (avg)	NPi (avg)
NBCi \leq 2 + ANV \leq 2 (N = 13)	1.07	1.42	0.27
NBCi \leq 2 + ANV $>$ 2 (N = 10)	1.48	3.42	0.44
NBCi $>$ 2 + ANV $>$ 2 (N = 22)	3.03	2.96	0.38

analysis of the Ni and NBCi. Selection of patients for study required provision of reliable 24-hr voiding data, a reflection of the difficulty with which elderly outpatients perform such self-evaluations. Of these, 13 had mild and 32 had severe nocturia by diary criteria; 20 had mild and 25 had severe nocturia in response to AUASS question #7 (Table II).

In the case of AUASS question #7 (degree of nocturia), the odds of having a severe AUA #7 response was found to be 4.09 times higher for patients with an NBCi $>$ 2.0 compared with patients whose NBCi was \leq 2.0 using logistic regression analysis. Accordingly, we carried out detailed comparisons of three major patient groups' diary-mediated nocturia severity categories: group 1 = NBCi \leq 2 + ANV \leq 2; group 2 = NBCi \leq 2 + ANV $>$ 2; group 3 = NBCi $>$ 2 + ANV $>$ 2 (Table II).

In comparing patients with severe nocturia but near-normal NBC (NBCi \leq 2, group 2) with those having mild nocturia and near-normal NBC (NBCi \leq 2, group 1), Ni was superior to NPi in identifying nocturnal urine overproduction as the suspected explanation for their nocturia (Ni = 3.42 vs. 1.42, P = 0.0002 cf. NPi = 0.44 vs. 0.27, P = 0.018, Mann-Whitney test, respectively).

Group 3 describes a subset of patients having severe nocturia selected for at least severely diminished NBC (avg. NBCi = 3.03). In this group, both putative indices of nocturnal urine overproduction behaved in a similar fashion: The mean Ni in this group was 2.96 (diminished from its value of 3.42 in group 2 whose principal etiology of nocturia lies in NP); the mean NPi diminished similarly from 0.44 in group 2 to 0.38 in group 3. However, these parallel drops in both the Ni and NPi failed to reach statistical significance (P = 0.76 for Ni [group 3]/Ni [group 2]; P = 0.81 for NPi [group 3]/NPi [group 2]; Mann-Whitney test).

Only five of 45 (11%) patients in this series had an FBC greater than the NUV (Ni $<$ 1). Of these, four of five (80%) were categorized as having mild nocturia by diary analysis.

Table III describes the effects of specific urodynamic diagnoses of detrusor instability, bladder outlet obstruction, sensory urgency, and impaired detrusor contractility on the NBCi. There were no significant differences in mean NBCi whether these diagnoses were present or not.

DISCUSSION

Nocturia refers both to the simple notion of urination 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 voided, or to the number of occasions on which urine is passed. What constitutes an excessive frequency or volume for nocturnal urination has not been well defined for any age group and certainly not for the elderly [Hennessey and Shen, 1986; Shah, 1994].

TABLE III. Correlation of Mean NBCi With Presence or Absence of Specific Urodynamic Diagnoses

Urodynamic Dx	Mean NBCi	No. of patients	Standard error	<i>P</i> value (Mann-Whitney)
(+) DI	2.18	10	0.28	
(-) DI	2.13	35	0.22	0.7954
(+) BOO	2.15	27	0.24	
(-) BOO	2.13	18	0.28	0.9354
(+) SU	2.56	7	0.56	
(-) SU	2.06	38	0.19	0.6163
(+) IDC	2.30	13	0.47	
(-) IDC	2.08	32	0.17	0.8120

Dx, diagnosis; DI, detrusor instability; BOO, bladder outlet obstruction; SU, sensory urgency; IDC, impaired detrusor contractility.

There are three broad categories of pathophysiology that account for nocturia, which we defined here: a) NP, b) diminished NBC (elevated NBCi), and c) mixed (combination of a and b). The NP syndrome was defined by Asplund [1995] as increased urine output during the night. However, in contrast to diabetes insipidus (in which both intake and output are increased), 24-hr urine production remains normal, indicating a variation in normal diurnal production of urine. This increased nocturnal diuresis results in NUV in excess of bladder capacity, creating the need for night-time micturition in the form of either nocturnal enuresis or nocturia [Norgaard, 1991].

Several definitions of NP have been used, such as NUV >6.4 mL/kg [Matthiesen et al., 1996], NUV exceeding one third of the total daily urine output, and a nocturnal diuresis of ≥ 0.9 mL/min, but none has met with widespread acceptance [Saito et al., 1993]. Of paramount importance is the voiding diary, without which the differential diagnosis of nocturia cannot be made. On the basis of the voiding diary, the patient is categorized as having NP, diminished NBC, or a mixed disorder. The workup for various causes of NP include history and physical and laboratory examinations designed to evaluate the patient for symptoms and signs of congestive heart failure, diabetes, renal insufficiency, venous stasis, postural edema, etc. When diabetes insipidus is suspected, water deprivation or solute loading tests may be used [Adam, 1997]. Workup for etiology of increased NBCi is more related to endoscopic and urodynamic techniques for diagnosing vesical inflammatory, neoplastic, or functional disorders. Remediable medical causes of NP should be identified and treated, but in some instances nocturia persists and in most patients clearly identifiable remediable conditions are not found. Empirical treatment options include evening fluid restriction (a form of behavior modification), timed diuretics [Pedersen and Johansen, 1988; Reynard et al., 1998], afternoon naps, application of compressive stockings when appropriate, and anti-diuretic hormone administration [Sommer et al., 1990; Griffiths et al., 1992; Saito et al., 1993; Donahue and Lowenthal, 1997]. Treatment of diminished NBC is directed at its underlying cause.

Since elevated NBCi by definition involves NBC, which is less than FBC, investigation as to the cause (if any) of this discrepancy is warranted. Specific treatment of the underlying urologic condition would then be expected to have a mitigating effect on nocturnal bladder undercapacity as a component of nocturia.

A potentially useful point for further study would entail voiding diary data in an age- and sex-matched elderly population without nocturia. Such a study would evalu-

ate normal ranges for both functional and nighttime bladder capacities. The relationship between FBC, NBC, and the various nocturia indices is currently being studied by our group. Indeed, deviation of patients' FBC from the norm may help to classify further nocturia and validate the use of the nocturia indices presented here.

For many elderly men, prostatism is considered to be the primary cause of their nocturia, often despite insufficient investigation. Therapy for these patients often involves surgery, which reduces problems associated with obstruction such as poor stream and incomplete voiding, but often does little to reduce the more irritative symptoms such as nocturia and frequency. Thus, whereas Bruskewitz et al. [1986] reported improved voiding symptoms such as nocturia in 75% of patients 3 years after prostate surgery, 25% experienced little or no improvement and half of these worsened as a result.

Patients demonstrated by diary analysis to have both NP and increased NBCi should have an assessment of the predominant cause of nocturia. Thus, for example, if a patient is found to have an NBCi of 0.8 and relative nocturnal urine overproduction to the extent that the Ni is greatly in excess of 1.5, treatment of the nocturnal urine overproduction should be prioritized and would be expected to provide a greater benefit to symptomatic nocturia than would a strategy to diminish the contribution from diminished NBC. As a generalization, we recommend initial treatment of NP since it does not involve invasive or potentially irreversible treatment such as surgical procedures intended to affect obstructive uropathy.

We recently reviewed the records of 194 consecutive patients with nocturia: 129 women and 65 men ranging in age from 17 to 94 years [Weiss et al., 1998]. Overall, 13 (7%) had NP, 111 (57%) increased NBCi, and 70 (36%) had a mixed etiology of their nocturia (both NP and increased NBCi). Forty-five (23%) also had polyuria. Our study confirmed that the etiology of nocturia is multifactorial, and (as in the present report) in many instances unrelated to the underlying urologic condition such as benign prostatic hyperplasia, urge or stress incontinence, and detrusor instability. Nocturnal overproduction of urine was found to be a significant component of nocturia in 43% of the patients studied. Rational care of the patient with nocturia therefore entails the concept that its treatment should be directed at both conditions.

In the present study, there was a strong statistical correlation between severe responses to AUASS question #7 and an NBCi >2, a correlation useful in determining at what value the NBCi should trigger evaluation of nocturnal lower urinary tract dysfunction in patients being investigated for nocturia. Thus, we suggest a cutoff point of NBCi >2 as highly significant in defining diminished NBC as a factor in the etiology of nocturia. This discriminant was then used in testing the hypothesis that the Ni is a reliable indicator of nocturnal urine overproduction relative to maximal bladder capacity as a major etiology of nocturia: here, one must control for NBC status. Thus, analysis of the difference between groups 1 and 2 is critical in that both groups are statistically similar with regard to having low NBCi (NBCi ≤2), whereas group 1 patients are selected for having mild nocturia (by diary) and group 2 patients, severe nocturia. The explanation for nocturia in group 2 must therefore be nocturnal urine overproduction. Clearly, a putative index of nocturnal urine overproduction must yield a significant increase from group 1 to group 2. The Ni did indeed behave in such a fashion, in fact better than the NPi (see Table II).

The lack of a relationship between the presence or absence of specific urodynamic diagnoses and the NBCi (Table III) suggests that there may be factors causing

diminished NBC other than those that may be diagnosed during a waking urodynamic study. For example, it may be necessary to perform combined nocturnal urodynamic and sleep studies to prove the existence of detrusor instability as a cause for nighttime voiding or perhaps to find whether patients first awoken due to a primary sleep disturbance, then proceed to nighttime micturition.

The majority of the small subset of patients in this series having an Ni <1 had mild nocturia (four of five). Thus the question is raised as to what value of Ni serves as a practical threshold between normal and excessive nocturnal urine output. Although it would seem intuitively that an Ni >1 indicates relative nocturnal urine overproduction where nocturnal urine volume is greater than FBC, our data reveal that in the group of patients analyzed with mild nocturia (ANV \leq 2) and low NBCi, the average Ni was 1.42. Based on these data, we propose an Ni of 1.5 to be a transition point greater than which a diagnosis of relative nocturnal urine overproduction may be made in determination of the etiology of nocturia.

CONCLUSIONS

The Ni and NBCi are sensitive measures of nocturnal urine overproduction and diminished NBC, respectively. This study demonstrates the utility of these indices as complementary quantifiers of the genesis of nocturia in men. The data suggest a threshold of NBCi >2 as highly significant in defining diminished NBC as a factor in the etiology of nocturia. As a complement to the NBCi, we propose an Ni of 1.5 to be a practical discriminant greater than which a diagnosis of nocturnal urine overproduction relative to bladder capacity may be made in determination of the etiology of nocturia.

REFERENCES

- Adam P. 1997. Evaluation and management of diabetes insipidus. *Am Fam Physician* 55:2146.
- Asplund R. 1995. The nocturnal polyuria syndrome (NPS). *Gen Pharmacol* 26:1203.
- Bruskewitz RC, Larsen EH, Madsen PO, Dorflinger T. 1986. 3-year follow-up of urinary symptoms after transurethral resection of the prostate. *J Urol* 136:613.
- Donahue JL, Lowenthal DT. 1997. Nocturnal polyuria in the elderly person. *Am J Med Sci* 314:232.
- Griffiths DJ, McCracken PN, Harrison GM, Gormley EA. 1992. Characteristics of urinary incontinence in elderly patients studied by 24-hour monitoring and urodynamic testing. *Age Ageing* 21:195.
- Hennessy CH, Shen JKM. 1986. Sources of unreliability in the multidisciplinary team assessment of the elderly. *Eval Rev* 10:178.
- Matthiesen TB, Rittig S, Nørgaard JP, Pedersen EB, Djurhuus JC. 1996. Nocturnal polyuria and natriuresis in male patients with nocturia and lower urinary tract symptoms. *J Urol* 156:1292.
- Nørgaard JP. 1991. Pathophysiology of nocturnal enuresis. *Scand J Urol Nephrol Suppl* 140:13.
- Pedersen PA, Johansen PB. 1988. Prophylactic treatment of adult nocturia with bumetanide. *Br J Urol* 62:145.
- Reynard JM, Cannon A, Yang Q, Abrams P. 1998. A novel therapy for nocturnal polyuria: a double-blind randomized trial of furosemide against placebo. *Br J Urol* 81:215.
- Rollema H. 1994. Clinical significance of symptoms, signs, and urodynamic parameters in benign prostatic hypertrophy. In: Krane RJ, Siroky MB, Fitzpatrick JM, editors. *Clinical urology*. Philadelphia: Lippincott. p 859–60.

- Saito M, Kondo A, Kato T, Yamada Y. 1993. Frequency-volume charts comparison of frequency between elderly and adult patients. *Br J Urol* 72:38.
- Shah PJR. 1994. The assessment of patients with a view to urodynamics. In: Mundy AR, Stephenson TP, Wein AJ, editors. *Urodynamics—principles, practice and application*. Edinburgh: Churchill-Livingstone. p 85–93.
- Sommer P, Nielsen KK, Bauer T, Kristensen ES, Hermann GG, Steven K, Nordling J. 1990. Voiding patterns in men evaluated by a questionnaire survey. *Br J Urol* 65:155.
- Weiss JP, Stember DS, Blaivas JG. 1998. Nocturia in adults: classification and etiology. *Neurourol Urodynam* 17:467–72.