

# Long-Term Followup of Children with Nocturnal Enuresis: Increased Frequency of Nocturia in Adulthood

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## Abbreviations and Acronyms

LUTS = lower urinary tract symptoms

NE = nocturnal enuresis

NMNE = nonmonosymptomatic nocturnal enuresis

OAB = overactive bladder

UI = urinary incontinence

Accepted for publication December 24, 2013. Supported by Ferring, Pfizer and Bard. This was unrestricted funding, with no interference in protocol, execution of trial, analysis or interpretation of results.

Study received institutional ethical committee approval (EC 2011/817).

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**Purpose:** We investigated the long-term prognosis of a cohort of children with nocturnal enuresis, and identified the prevalence of nocturia and persistent comorbid symptoms.

**Materials and Methods:** A questionnaire was sent to 1,265 patients treated for nocturnal enuresis during childhood at our university hospital. We used a validated tool, the International Consultation on Incontinence Modular Questionnaire on overactive bladder and urinary incontinence, to evaluate the presence of current urological symptoms. Participants were also asked about treatment received for nocturnal enuresis, and their medical files were analyzed.

**Results:** A total of 516 patients (41%) returned the questionnaire. Mean age was 17 years, and 64% of patients were male. Current urgency, daytime frequency and urinary incontinence were reported by 17%, 8% and 25% of patients, respectively. During the period of nocturnal enuresis up to 60% of patients had concomitant daytime symptoms. Nocturia was reported by 182 participants (35%). Males comprised 56% of patients (101) with nocturia and 69% of patients (230) without nocturia. Prevalence of current daytime symptoms and incontinence was higher in patients with nocturia ( $p < 0.001$ ). Those with nocturia were older at resolution of nocturnal enuresis ( $p < 0.001$ ) and suffered more non-monosymptomatic nocturnal enuresis ( $p < 0.014$ ).

**Conclusions:** About a third of patients experience nocturia, a fourth still report some kind of urinary incontinence, a fifth have regular urgency and a tenth have daytime frequency. Thus, resolution of nocturnal enuresis does not necessarily mean resolution of the underlying pathological condition. Some patients with nocturia who continue to suffer with bothersome symptoms might benefit from continuous treatment for the underlying condition.

**Key Words:** lower urinary tract symptoms, nocturia, nocturnal enuresis, prevalence

NOCTURNAL enuresis is a bothersome condition with a high prevalence in children, affecting up to 10% of 7-year-old children and decreasing to a rate of approximately 0.5% in adults.<sup>1</sup> This decrease in incidence has led to the misconception that

nocturnal enuresis is a benign disorder that resolves spontaneously. Yeung et al documented that in children with severe enuresis the spontaneous resolution rate is only 50% to 60%.<sup>2</sup> These results refer to non-treated patients in Hong Kong and,

therefore, are hard to extrapolate to a Western setting, where a majority of patients will search for medical and nonmedical treatment options. The few studies describing long-term prognosis for nocturnal enuresis do not comply with the new International Children's Continence Society standardization terminology and are not in line with the actual diagnostic and therapeutic approach, which makes extrapolation of these results to the current clinical setting difficult.<sup>3</sup>

Nocturia, or the complaint of having to wake at night once or more to void (International Continence Society definition), has a prevalence of 4% in healthy school children but clearly increases with age up to a 50% prevalence in individuals older than 50.<sup>4,5</sup> This symptom is often underreported and underestimated in pediatric enuresis studies.

It is widely accepted that the main difference between NE and nocturia is the presence of appropriate arousal to stimuli of the bladder.<sup>6</sup> Although there are obvious dissimilarities in prevalence and expression between nocturia and enuresis, similarities regarding etiology, comorbidities and treatment suggest overlap in the pathogenesis.<sup>7</sup> However, data are lacking on how many patients have resolution of enuresis by switching from enuresis to nocturia. Susceptibility to nocturia in patients with enuresis or a history of enuresis in patients with nocturia has been studied, although mostly in small cohorts.<sup>8,9</sup>

We investigated the long-term prognosis of a cohort of children with NE treated at a specialized multidisciplinary enuresis center. The aim was to identify the prevalence of nocturia and persistent comorbid symptoms such as daytime incontinence and urgency.

## METHODS AND MATERIALS

### Study Design

We initiated an observational study in February 2012 by sending a questionnaire to a sample of 1,318 patients treated during childhood for NE at the departments of pediatric nephrology and urology of Ghent University Hospital. A total of 53 questionnaires were returned blank because of a wrong address, and so an estimated 1,265 patients received the questionnaire. Inclusion criteria were presentation with NE more than 5 years previously at a specialized multidisciplinary enuresis center. Patients with an obvious underlying condition explaining the incontinence and those still in followup in the last 3 years were excluded. The study aimed to target the group considered cured of NE.

To evaluate the current presence of nocturia and other urological symptoms such as urgency and UI, validated questionnaires were used, including the International Consultation on Incontinence Modular Questionnaire on OAB and UI. Participants were also asked about the

treatment they had received for NE. Questionnaires were mailed with an introductory letter and a prestamped envelope. Patients who had not responded by July 2012 were contacted by telephone and, if willing to participate, the questionnaires were sent again. This study was approved by the ethical committee of Ghent University (EC 2011/817).

Nocturia was defined according to 2 definitions, the standard definition of waking up once or more to urinate during the night, and the clinical definition of waking up twice or more. Patients were considered to have urgency if they answered "sometimes," "most of the time" or "all of the time" to the question, "Do you have to rush to the toilet to urinate?" They were considered to have daytime frequency when answering "more than 8 voids per day" to the question, "How many times do you void during the daytime?" The presence of UI and specific type of incontinence were evaluated through "yes/no" questions. Frequency of unwanted UI was subdivided as "once or less per week, 2 to 3 times per week, once a day or more than once a day." To evaluate related bother due to symptoms, a score of 0 to 10 was assigned, with 0 referring to no bother at all and 10 a great deal of bother. These questions were part of the International Consultation on Incontinence Modular Questionnaire on OAB and UI.

To evaluate the symptoms of patients suffering NE, the medical files of patients who returned the questionnaire were checked. Presence of daytime symptoms, primary or secondary enuresis and treatment were noted if available. NMNE was defined according to the old and new definitions, ie presence of concomitant daytime incontinence and presence of any concomitant LUTS, respectively.<sup>3</sup> If urgency was reported without any other LUTS and without a severity score, it was not considered a daytime symptom since clinical relevance was questionable.

### Statistical Analysis

Descriptive statistical analysis included Mann-Whitney U test for ordinal variables and Pearson chi-square test for categorical variables. Logistic regression analysis was used to map the associations between variables. A p value of less than 0.05 was considered statistically significant. All statistical procedures were performed with SPSS®, version 19.0 and Excel®.

## RESULTS

### Patient Characteristics

The questionnaire was returned by 516 patients (41%), with 389 (75%) responding to the first questionnaire and 127 (25%) following a reminder. Mean followup was 7 years (range 3 to 14). Mean age was 17 years, and 64% of patients were male. Males comprised 63% of the quick responders and 68% of late responders ( $p = 0.390$ ). Current urgency, daytime frequency and UI were reported by 17%, 8% and 25% of patients, respectively. During the period of NE up to 60% of patients had concomitant daytime symptoms (table 1). Nocturia was reported by 182 patients (35%). A total 157 patients (86%)

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