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Nocturia in mothers and enuresis in children: Possible links

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ABSTRACT

Objective: The aim of the present study was to examine the relationship between nocturnal enuresis (NE) of childhood and nocturia of parents.

Material and methods: The study was conducted across the network of general pediatricians of the ASL NA 1 of Naples, Italy. All the children with NE and their mothers were invited to attend the clinic for the study. Data were collected by personal interview. A 5-day bladder diary was collected from all the children. The mothers with nocturia were given a 3-day frequency-volume chart to assess the presence of nocturnal polyuria or reduced bladder capacity. Both children and mothers underwent a bladder ultrasound scan to measure the bladder wall thickness.

Results: A total of 224 mothers (aged between 23 and 45 years, average 33.3±4.1 years) and their 225 children (aged between 7 and 13 years, average 8.35±1.81 years) were investigated. Of the 224 mothers, 90 (40%) had nocturia, of which 55 (61%) clearly remembered that they had suffered from NE in childhood. Only 4 (11%) out of the 35 women without nocturia had NE ($p<0.001$). Children with persistence of NE beyond 11 years were more likely to have a parent with nocturia. Children with non-monosymptomatic NE were more likely to have mothers with nocturia (odds ratio (OR) 1.7, 95% confidence interval (CI) 1.2-7.1, $p<0.01$) or overactive bladder symptoms (OR 1.9, 95% CI 1.1-15.2, $p<0.01$).

Conclusion: These data suggest that there is a link between NE in childhood and nocturia in adulthood. A strong relationship was found between overactive bladder in children and overactive bladder in their mothers.

Keywords: Enuresis; family linkage; nocturia.

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Introduction

Nocturnal enuresis (NE) is defined as a complaint of intermittent incontinence that occurs during the main sleep period in children older than 5 years, and it affects up to 10% of 7-year-old children.[1] Nocturia is a common and often neglected symptom of adulthood, and although it is usually associated with elderly people, over 15% of men and women between 20 and 40 years present with this symptom.[2]

Enuresis and nocturia share many of the underlying pathophysiological mechanisms, such as nocturnal polyuria and decreased nocturnal bladder capacity. Moreover, there are clear similarities with respect to comorbidities and treatment. Previous studies showed that children with enuresis are more likely to experience nocturia and lower urinary tract symptoms in adulthood.[3] Moreover, parents of children with enuresis and overactive children had similar symptoms in their own childhood.[4,5]

However, these studies were mainly based on self-reported questionnaires and did not include the assessment of the underlying pathophysiological mechanisms. This can be extremely important to identify and promptly treat conditions that are the cause of debilitating symptoms that manifest themselves in adults.

Currently, there is emerging evidence showing the importance of a personalized therapy to increase the chances of success with regard

to NE and nocturia.[6-9] Therefore, a better understanding of the pathophysiology of NE and nocturia can be certainly important for a targeted therapeutic approach.

We examined the relationship between NE of childhood and nocturia of parents. We also investigated the link between the presence of lower urinary tract symptoms, such as urgency, incontinence, urge–incontinence, frequency in childhood, and the same symptoms in adulthood.

Material and methods

This study was conducted across the network of general pediatricians of the ASL NA 1 of Naples, Italy. The study protocol was approved by the ASL NA 1 Ethics Committee (41-01-2018). Data were collected by personal interview. Written informed consent was obtained from the parents or legal representatives of the infants.

All the children with NE and their mothers were invited to attend the clinic for the study. Inclusion criteria were the presence of monosymptomatic or non-monosymptomatic NE (NMNE) in children aged ≥6 years. NMNE was considered in children with enuresis and any other lower urinary tract symptoms, whereas enuresis in a child without any lower urinary tract symptoms was considered monosymptomatic enuresis.[10] For each child, the number of wet nights, the presence of daytime voiding symptoms (urgency, urge–incontinence, incontinence, holding maneuvers, and frequency), life-style regarding fluid intake, the presence of constipation, and any history of urinary tract infections were assessed.

For each parent, we assessed whether they had suffered from NE during childhood and whether there were daytime voiding symptoms (urgency, urge–incontinence, incontinence, holding maneuvers, and frequency). We also investigated at what age they stopped wearing daytime or nighttime diaper. We then asked about whether there were still daytime voiding symptoms (urgency, urge–incontinence, incontinence, holding maneuvers, and frequency) and whether there was nocturia. Nocturia was defined as the number of episodes per night urine was passed during the main sleep period.[1] Having woken to pass urine for the first time, each urination had to be followed by sleep or the intention to sleep[1]. We also assessed life-style regarding fluid intake, the presence of constipation, any history of urinary tract infections, difficulty in passing urine, the presence of nighttime incontinence, and pain before micturition, during micturition, or after micturition.

For all the children, a 5-day bladder diary was collected. Nocturnal diuresis had been measured by summing the nocturnal wet diapers weight (minus the weight of dry diapers) and the milliliter of the first morning void.[10] The nocturnal diuresis for five wet nights was evaluated. Nocturnal polyuria was defined as nocturnal urine production >130% of the expected bladder capacity.[9] All the women with nocturia were given 3-day frequency–volume charts. We assessed the presence of nocturnal polyuria based on a nocturnal polyuria index >0.33.[11] Reduced bladder capacity was defined as having both a nocturnal bladder capacity index >1.3 and a nocturnal polyuria index ≤0.33.[11]

Women who had any conditions explaining the nocturia and lower urinary tract symptoms, such as cerebral or spinal injury, major pelvic organ prolapse, diabetes mellitus and diuretics, antidepressant therapy, or in case they had completed <2 frequency volume chart entries were excluded from the study. Children were excluded if they had diagnosed urinary tract infection, diabetes mellitus, diabetes insipidus, neurogenic bladder, tethered cord syndrome, ectopic ureter, and psychological disorder, such as attention deficit hyperactivity disorder, or if they had completed a bladder diary for <2 days.

Both children and mothers underwent a bladder ultrasound scan. Bladder volume and bladder wall thickness were measured when the patients reported the first urge (full and ready to void). After the patients voided then, an ultrasound scan was repeated to measure bladder wall thickness of the empty bladder and the post-void residual volume. The bladder was considered empty when it contained <10% of its normal capacity. The bladder wall thickness was measured as the average of three measurements (anterior, posterior, and lateral). These parameters were measured perpendicular to the luminal surface, taking care not to include the vagina, rectum, or peritoneal reflection of the bladder dome.[12] The ultrasound scan was performed by using a 5-MHz frequency probe.

Statistical analysis

IBM Statistical Package for the Social Sciences Statistics 23 (IBM SPSS Corp., Armonk, NY, USA) was used for statistical analyses. Mann–Whitney U test was used for comparing ordinal variables, and Pearson chi-square test was used for comparing categorical variables. Logistic regression analysis was used to assess the associations between variables. A p value of <0.05 was considered statistically significant.

Results

Overall, 287 mothers and 285 children with NE were recruited into the study. Of the 287 mothers, 42 (15%) were excluded because they could not remember clearly details about whether

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they had suffered from NE in childhood. The other 21 mothers were excluded because of a history of cardiac disease (n=5), diabetes mellitus (n=6), and recurrent cystitis (n=10).

After the exclusion of these participants, 224 mothers and their 225 (88 boys and 137 girls) children were investigated. The ages of the mothers and their children were between 23 and 45 (average 33.3±4.1) years and between 7 and 13 (average 8.35±1.81) years, respectively. Ninety (40%) mothers had nocturia, of which 55 (61%) clearly remembered that they had suffered from NE in childhood. Only 4 (11%) out of the 35 women without nocturia had NE (p<0.001) (Table 1).

Of the 55 women with nocturia and NE in childhood, 32 (59%) remembered having NMNE. In this group of 32 nocturic women, enuresis in childhood disappeared on average at aged 11.72 years. Of the 4 women without nocturia who had NE in childhood, only 1 woman suffered from NMNE, which disappeared at 8 years. The prevalence of urgency, daytime frequency, and urinary incontinence was significantly greater in patients with nocturia than in those without (Table 1).

Table 1. Patient characteristics

	Mothers with nocturia (n=90)	Mothers without nocturia (n=134)	p
Median years, age (range)	35.3±3.1	32.2±3	>0.05
No. of daytime symptoms (%)			
Urgency	31 (34)	13 (10)	<0.001
Frequency	16 (18)	4 (3)	<0.001
Urinary incontinence	35 (39)	21 (16)	<0.001
Primary nocturnal enuresis	55 (61)	4 (3)	<0.001
Non-monosymptomatic NE	32 (35)	1 (1)	<0.001
No. of voids/night			
1	80 (89)	–	–
2	6 (7)	–	–
3	4 (4)	–	–
Children with NMNE	53 (59)	43 (32)	<0.001
Children with MNE	37 (41)	92 (68)	<0.001

NMNE: non-monosymptomatic nocturnal enuresis; MNE: monosymptomatic nocturnal enuresis

Bladder diary measurements of the mothers with and without nocturia and their children are shown in Table 2. Mothers with nocturia had a significantly lower maximum voided volume and higher nocturnal urine production than those without nocturia (Table 2). When we considered nocturic women who suffered from NMNE in childhood, they had higher risk of having overactive bladder symptoms and bladder wall thickness of the empty bladder >5 mm (odds ratio (OR) 3.1, 95% confidence interval (CI) 1.9–12.3, p<0.05) or reduced bladder capacity (OR 4.2, 95% CI 1.5–11.4, p<0.01) in adulthood. Children with persistence of NE beyond 11 years were more likely to have mothers with nocturia. Specifically, for every year of age beyond 11 years, the OR for having a parent with nocturia increased by 0.19.

Ninety-six (43%) out of 225 children had NMNE, whereas 129 (57%) had monosymptomatic NE. Bladder wall thickness was significantly higher in children with NMNE, and their bladder capacity was significantly lower than in children with MNE (Table 3).

The prevalence of NMNE was significantly higher in the group of children of nocturic mothers (53 (59%) vs. 43 (32%), respectively, p<0.001) (Table 1). Children with NMNE had higher probability of having their mothers with nocturia (OR 1.7, 95% CI 1.2–7.1, p<0.01), overactive bladder symptoms (OR 1.9, 95% CI 1.1–15.2, p<0.01), or reduced bladder capacity (OR 2.7, 95% CI 1.5–10.6, p<0.01). When we examined the children with NMNE who also had bladder wall thickness >5 mm (empty bladder) (n=53), the OR of having their mother with nocturia increased to 2.5 (OR 2.5, 95% CI 1.5–10.1, p<0.01). Children with NMNE also had higher risk of having their mother with

Table 2. Bladder diary measurements in children and mothers

	Mothers with nocturia (n=90)	Mothers without nocturia (n=134)	p[a]	Children with NMNE (n=96)	Children with MNE (n=129)	p[b]
Nocturnal urine production, mL	701 (148)	615 (128)	0.03	186 (114)	306 (168)	<0.001
Maximum voided volume, mL	324 (162)	408 (132)	0.04	205 (124)	291 (116)	0.08
No. of voids/24 h	6.5 (2)	5.6 (1)	0.08	7.0 (1.5)	5.4 (1.0)	<0.001
24-hour urine volume, mL	1900 (347)	2200 (268)	0.02	880 (264)	1347 (327)	<0.001

Data are presented as mean (SD). [a]Comparison of mothers with against those without nocturia. [b]Comparison of children with NMNE against those with MNE. NMNE: non-monosymptomatic nocturnal enuresis; MNE: monosymptomatic nocturnal enuresis

Table 3. The mean (SD) of the bladder volume and bladder wall thickness in children and mothers

	Mothers with nocturia (n=90)	Mothers without nocturia (n=134)	p[a]	Children with NMNE (n=96)	Children with MNE (n=129)	p[b]
Bladder wall thickness, mm (full bladder)	2 (0.8)	1.3 (0.5)	0.001	2.1 (0.7)	1.2 (0.6)	0.001
Bladder wall thickness, mm (empty bladder)	4.2 (1.4)	2.6 (0.4)	<0.001	5.3 (0.5)	2.9 (0.6)	<0.001
Bladder volume mL, first urge (full and ready to void)	284 (146)	398 (161)	0.01	188 (180)	262 (156)	0.01

[a]Comparison of mothers with against those without nocturia. [b]Comparison of children with NMNE against those with MNE. NMNE: non-monosymptomatic nocturnal enuresis; MNE: monosymptomatic nocturnal enuresis

more than one episode of nocturia (OR 2.6, 95% CI 1.2–15.1, p<0.01). A significant correlation was not found between nocturnal polyuria in children and in mothers (p>0.05).

Discussion

The present study shows a strong link between childhood NE and nocturia in adulthood. We found that children with persistence of NMNE beyond 11 years have a higher probability of having their mother with nocturia and with overactive bladder. We also showed a strong relationship between overactive bladder in children and overactive bladder in mothers. However, the same correlation was not found with regard to nocturnal polyuria.

Different studies previously assessed whether NE in childhood and urinary incontinence or nocturia in adulthood shared the same causes.[13,14] These studies were based on self-reported questionnaires and showed that a history of NE and childhood urinary symptoms increased the risk of having urinary incontinence and overactive bladder symptoms in adulthood. However, these studies did not include the specific assessment of the etiology by using frequency–volume charts or bladder ultrasound scan.

Our findings show that in case of NMNE in childhood, there is a three times higher risk of having overactive bladder syndrome in adulthood. This is in agreement with Montaldo et al.'s [4] results showing a close link between nocturia in adulthood and NE in childhood. In their study, they assessed the data collected by self-reported questionnaires of 250 mothers of enuretic children and showed that over half of the mothers with nocturia and NE in childhood had daytime voiding problems. However, the assessment of neither bladder capacity nor bladder wall thickness and nocturnal polyuria was performed.

Yazici et al.[15] instead showed, in a group of 682 female nursing students aged between 17 and 24 years, no relationship between NE in childhood and nocturia. However, as NE severity increased, the relationship between nocturia and NE became more relevant. There are important differences between our study and that by Yazici et al.[15] First, the study design is different since we recruited a specific group of patients (mothers of enuretic children). Second, the mean age of our study group was older.

More recently, Goessaert et al.[3] investigated the long-term follow-up of children with NE in a large cohort of 516 patients and showed that despite the resolution of NE, a third of patients go on to experience nocturia and a fourth of them still report lower urinary tract symptoms. These data may reflect that the resolution of NE does not necessarily mean the resolution of the underlying pathological condition. Our data support these findings and underline the need for a prompt treatment of overactive bladder syndrome.

Our study showed that the group of nocturic women was older at the age of cure of enuresis than the group without nocturia. These data highlight that the more severe the NE, the higher is the probability of nocturia. This is in agreement with the study by Goessaert et al.[3] who showed that the age at cure of NE was significantly greater in the nocturia group. The authors found that after the age of 10 years, the cure rates of bladder dysfunction decrease, and a significant number of patients continue to have lower urinary tract symptoms. This underlines that a continuous treatment might be considered in case of children consulting a tertiary center for therapy-resistant NMNE. Nocturia is well known to reduce the quality of life and cause physiological injuries and mood disturbances.[2] Therefore, there is a concerted effort from the research community to decrease the prevalence of nocturia and promptly act on the risk factors contributing to the extent of this condition.

When we assessed the relationship between NE in children and nocturia in mothers, we found that in case of persistence of NE beyond 11 years, children were more likely to have a mother with nocturia. Montaldo et al.[4] previously also showed that in the most severe forms of NE, the probability of having a nocturic mother was significantly higher. Our study adds to these data

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that in case of a child with overactive bladder, the probability of having a parent with overactive bladder and reduced bladder capacity is significantly higher.

Family and twin studies have shown that lower urinary tract symptoms and enuresis are heritable with an autosomal dominant mode.[16] Our data are in keeping with these findings and highlight a close link between mothers' overactive bladder symptoms and those of their children. On the other hand, when we investigated whether there was any relationship between nocturnal polyuria in children and mothers, there was not any. These findings might reflect that nocturnal polyuria is not only caused by a disturbance in anti-diuretic hormone secretion pattern, which is genetically inherited, but other intra-individual factors play a role in the nighttime urine production.

In the present study, we also attempted to investigate the pathophysiological mechanisms of NE in children and nocturia in mothers. However, most of our data were extrapolated from bladder diaries and bladder ultrasound scans, thus limiting the explanation of pathophysiological mechanisms.

Despite that, the present data may pose a significant relevance in the clinical care. In fact, they highlight that pediatric lower urinary tract symptoms, such as urgency, frequency, incontinence, and urge–incontinence, might be considered as possible indicators of lower urinary tract dysfunction (i.e., overactive bladder) in adulthood. These findings suggest a prompt and continuous treatment of the most severe forms of overactive bladder syndrome and indicate that a longer follow-up is warranted to avoid bothersome urinary symptoms in adulthood.

In conclusion, the present study confirms the close link between nocturia in adulthood and NE in children and contributes to increase our knowledge on the possible long-term implications of low urinary tract dysfunction in childhood.

Ethics Committee Approval: Ethics committee approval was received for this study from the ethics committee of A.S.L. NA 1 (41-01-2018).

Informed Consent: Written informed consent was obtained from the parents or legal representatives of the infants.

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