

Nocturnal enuresis: prevalence and associated LUTS in adult women attending a urogynaecology clinic

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Abstract

Introduction Nocturnal enuresis (NE) is an underreported symptom with a profound impact on quality of life. The primary objective of this study was to investigate the prevalence of NE and its association with other lower urinary tract symptoms (LUTS).

Methods A validated pelvic floor questionnaire [electronic Personal Assessment Questionnaire–Pelvic Floor (ePAQ-PF)] was completed by 2302 women attending a urogynaecology clinic over a 3-year period. Association between NE and overactive bladder (OAB), stress incontinence (SUI) and nocturia was assessed using logistic regression. Subgroup analysis was performed on women with NE undergoing transvaginal tape (TVT). Ethical approval was acquired from the University of Sheffield and statistical analysis performed using SPSS version 22.

Results The overall prevalence of NE reported in the cohort was 23 % (536 women). The reporting of NE was significantly associated with OAB ($p < 0.005$), SUI ($p < 0.005$) and nocturia ($p < 0.005$). Of 84 women undergoing TVT, 49 % reported NE preoperatively. These women reported significantly more severe symptoms of SUI and OAB ($p < 0.05$). Sixty percent reported improvement or cure of NE postoperatively, and this was dependent on improvement or cure of SUI ($p < 0.005$). The presence of NE was a negative predictor

for improvement in symptoms of SUI following TVT ($p = 0.037$).

Conclusion This study provides insight into NE, a commonly reported symptom in women attending urogynaecology clinics. To our knowledge, this is the first study to implicate stress incontinence as an important aetiological factor in women with NE. Further studies are required to better understand the aetiology of NE in adult women and relate this to management and outcome.

Keywords Nocturnal enuresis · ePAQ · OAB · Nocturia · Stress incontinence · TVT

Introduction

Nocturnal enuresis (NE) is defined as involuntary loss of urine that occurs during sleep; it can be classified as either primary, persistent primary or secondary [1]. NE can be monosymptomatic or polysymptomatic [occurring with other lower urinary tract symptoms (LUTS)]. It is an underreported symptom with a profound impact on quality of life (QoL) [2]. Primary nocturnal enuresis (PNE) is defined as episodes of urinary incontinence (UI) during sleep in children ≥ 5 years of age [3]. The condition typically improves with advancing age, with reported prevalence of 16 % at 5 years falling to ~3 % and 2 % by the ages of 9 and 19, respectively [4]. PNE that fails to resolve by adulthood is termed persistent primary NE (PPNE), which has an estimated prevalence rate of 2.3 % in the adult population [5] and is associated with detrusor overactivity (DO) in 93 % of cases [6].

The standard International Continence Society (ICS) definition of secondary NE (SNE) in children is NE arising after a period of nighttime dryness of at least 6 months [3]. Adult SNE has been described as symptoms arising after 1 year of

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dryness [7]. There is a paucity of data on prevalence and aetiology of adult SNE in comparison with other types of NE. A questionnaire study of 13,081 respondents aged 18–64 years reported overall prevalence of NE of 0.5 % [2]; 50 % of men and 81 % of women were considered to have SNE. In a cohort study of 12,795 women with LUTS who underwent urodynamic studies, prevalence of SNE was 14.4 % [7]. That study observed that women with SNE were significantly more likely to report symptoms of overactive bladder (OAB) and nocturia, and the most significant urodynamic findings were low bladder capacity, DO incontinence and low maximal urethral closing pressure (MUCP).

The majority of research in this area has focussed on PNE in children and adolescents, with comparatively few studies investigating NE in adult women. To our knowledge, the prevalence of NE in women attending urogynaecology clinics has not been reported. The objectives of this study were to investigate the prevalence of NE and its association with other LUTS in a cohort of women referred to a urogynaecology clinic.

Methods

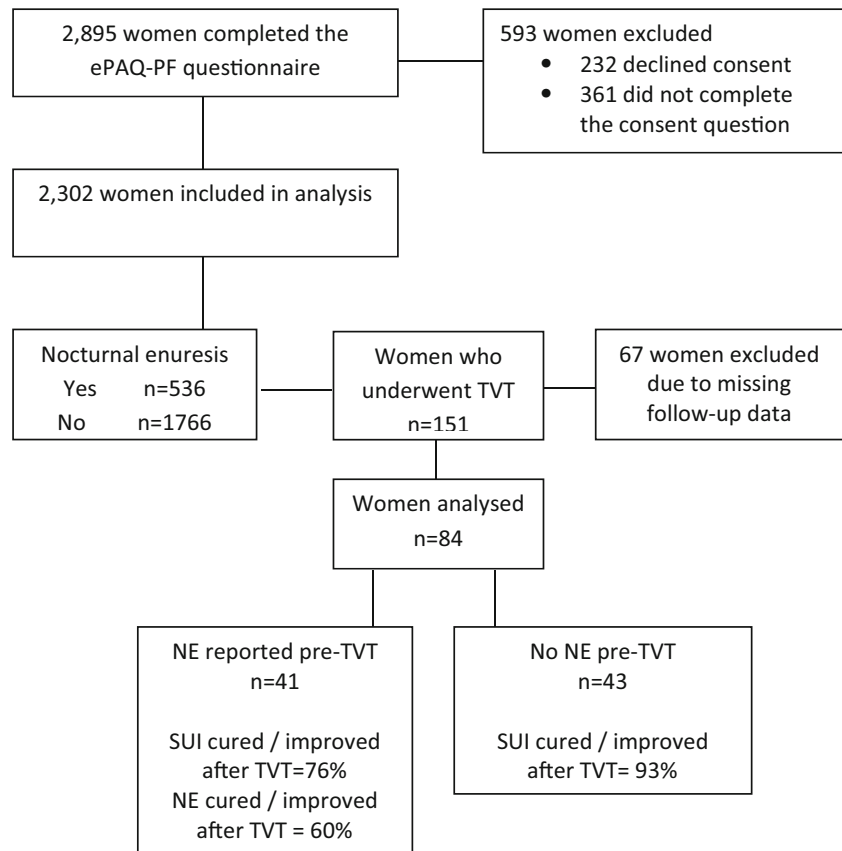
Between 2012 and 2015, 2895 women completed the electronic Personal Assessment Questionnaire–Pelvic Floor (ePAQ-PF) as part of their routine clinical care prior to their first consultation at a urogynaecology clinic. Two hundred and thirty-two women (8 %) declined consent for use of their anonymised data for further research, and a further 361 women (12 %) did not complete the consent question of the questionnaire, leaving 2302 women who were included in the analysis (Fig. 1). Ethical approval was obtained from the University of Sheffield (Ref 007395) and statistical analysis performed using SPSS (version 22).

The ePAQ-PF is a validated, web-based interactive questionnaire that provides an in-depth evaluation of a woman's pelvic floor symptoms and their impact upon her QoL [8–10]. The questionnaire can be completed online or using a touch-screen computer terminal in clinic. The 120-item questionnaire was designed to improve communication and detailed assessment by providing patients with an opportunity to report symptoms of an intimate and sensitive nature, many of which may be difficult to express face to face [11, 12]. The questionnaire covers dimensions of urinary, bowel, vaginal and sexual function. Within each dimension are four to five scored domains. Domain scores are derived by dividing the sum of all item scores in that domain by the total possible item score and multiplying this by 100 to produce a scale ranging from 0 to 100. On this scale, a score of 0 indicates the best and 100 indicates the worst possible health status. The following items from ePAQ-PF were assessed:

- Q₂₁ Do you suddenly get a strong urge to rush to the toilet to pass urine?
- Q₂₂ When you get the urge to go, does urine start to leak before you can make it to the toilet?
- Q₂₃ Does urine leak when you wash your hands or hear the sound of running water?
- Q₂₄ Does urine leak when you are opening or unlocking your door to your home?
- Q₂₆ During the night, how many times do you have to get up to urinate on average?
- Q₂₇ Does urine leak when you are asleep?
- Q₂₈ Does urine leak when you cough?
- Q₂₉ Does urine leak when you sneeze?
- Q₃₀ Does urine leak when you exercise, lift things, jump or run?
- Q₃₁ Does urine leak with movements such as standing up, bending down or getting dressed?
- Q₃₂ Does urine leak when you are walking?

Response options to Q₂₆ (frequency of nocturia) are converted to scores of 0, 1, 2, 3, 4 or 5, respectively. Response options for the remaining items are Never, Occasionally, Most of the time or All of the time and scored 0, 1, 2 or 3, respectively. Symptom impact is graded as Not a problem, A bit of a problem, Quite a problem or A serious problem and scored 0, 1, 2 or 3, respectively. OAB and stress incontinence (SUI) symptom domain scores are calculated from responses to Q_{21–24} and Q_{28–32}, respectively. A logistic regression model was used to explore the association of NE with symptoms of OAB, nocturia and SUI.

Subgroup analysis was performed on women with SUI who underwent transvaginal tape (TVT) to investigate whether treatment of SUI was associated with changes in symptoms of NE. Inclusion criteria were women who had undergone TVT between 2012 and 2015 and completed pre- and postoperative ePAQ-PF at 3 months' follow-up. Demographic details were collected from a standardised anaesthetic preoperative assessment including body mass index (BMI), smoking status, previous surgery for UI and diagnosis of depression, anxiety, diabetes or sleep apnoea. Urodynamic findings, ePAQ symptom score for nocturia and domain scores for bladder, bowel, vaginal and sexual function were compared between women with or without NE (unpaired, two-tailed *t* test). Impact of TVT on symptom domain scores for OAB and SUI (paired *t* test) and symptoms of nocturia and NE (Wilcoxon signed-rank test) were assessed. A linear mixed model was used to explore the association of changes in symptoms of OAB, SUI and nocturia on the reporting of NE following TVT. Improvement in SUI was classified as >50 % improvement in SUI domain score. Further analysis was performed to compare women who reported cure or improvement in NE with those who reported no change or worsening of NE. Questionnaire data and the results of preoperative urodynamic studies were compared between the two groups.

Fig. 1 Movement of women through the study

Results

The prevalence of NE in women attending the urogynaecology clinic was 23 % (536/2302 women). Mean age of women with and without NE was 54 (range 18–89) and 54 (range 17–94) years, respectively.

Association between NE and other LUTS

Symptoms of OAB ($p < 0.005$), SUI ($p < 0.005$) and nocturia ($p < 0.005$) were all shown to be significant and independent predictors of NE (Table 1). An increase in OAB domain score was associated with an increase in the odds of NE [odds ratio (OR) = 1.03, 95 % confidence interval (CI) 1.02–1.04]. An increase in SUI domain score was also associated with an increase in the odds of NE (OR = 1.04, 95 % CI 1.04–1.05). Patients who reported three or more episodes of nocturia were shown to have an OR of 2.99 (95% CI 1.94–4.61) for having NE compared with those who did not report nocturia.

Women undergoing TVT

One hundred and fifty-one women underwent TVT during the study period, of whom pre- and postoperative ePAQ-PF questionnaire data were available in 84 cases (56 %). NE was reported by 49 % of women ($n = 41$) preoperatively and was

significantly associated with higher BMI; smoking; higher symptom domain scores for OAB, SUI and voiding dysfunction; and greater impact of bladder symptoms on QoL and sexual function. Sixty-three women underwent preoperative urodynamic studies, 16 underwent TVT without urodynamic studies and data were unavailable in five cases. There was no significant difference in urodynamic findings between groups (Table 2).

TVT outcome

Following TVT, women reported significant improvements in OAB (−17.78, 95 % CI 11.45–24.11, $p < 0.005$) and SUI (−56.41, 95 % CI 46.06–66.77, $p < 0.005$) and significant reductions in episodes of nocturia ($p = 0.003$). Reported cure or

Table 1 Association of nocturnal enuresis (NE) with other lower urinary tract symptoms (LUTS) (logistic regression analysis)

LUTS	Association of NE with LUTS OR (95 % CI)	P value
OAB domain score	1.03 (1.02–1.04)	<0.005
SUI domain score	1.04 (1.04–1.05)	<0.005
Nocturia symptom score	2.99 (1.94–4.61)	<0.005

OAB overactive bladder, SUI stress urinary incontinence, OR odds ratio, CI confidence interval

Table 2 Women with or without nocturnal enuresis (NE) undergoing transvaginal tape (TVT): comparison of demographic details, comorbidities, preoperative ePAQ-PF symptom profiles and urodynamic findings

	Women with NE undergoing TVT <i>n</i> = 41	Women without NE undergoing TVT <i>n</i> = 43	<i>P</i> value
Mean age, years (range)	52 (33–83)	51 (34–78)	0.54
Mean BMI, kg/m ² (SD)	31.4 (5.9)	28.3 (5.3)	<0.05
Smoking	7/32	2/40	<0.05
ASA grade (mode)	2/32	1/40	0.06
Prior UI surgery	2/32	2/40	0.82
Diabetes	2/32	1/40	0.43
Sleep apnoea	5/32	4/40	0.52
Depression	5/32	7/40	0.83
Anxiety	1/32	2/40	0.69
OAB, mean score (SD)	39 (18.5)	24 (15.2)	<0.05
SUI, mean score (SD)	77 (17)	52 (17)	<0.05
Nocturia, mean score (SD)	1.7 (1.1)	1.4 (0.8)	0.17
Voiding dysfunction, mean score (SD)	21 (16.3)	12.1 (14.5)	<0.05
Bladder pain	12.9 (16.2)	10.5 (14.7)	0.48
Bladder QoL	86 (17)	63.6 (25.7)	<0.05
Irritable Bowel Symptoms	28.1 (20.1)	25.8 (20.7)	0.6
Constipation	19.3 (14.3)	26.2 (21)	0.12
Evacuation difficulty	17 (17)	21.1 (20.3)	0.49
Faecal incontinence	17 (13.9)	12.9 (12.5)	0.16
Bowel QoL	17.7 (28.5)	12.9 (20.9)	0.39
Vaginal pain	20.4 (22.3)	17.7 (21.6)	0.58
Vaginal capacity	6.9 (15.7)	7.9 (22.3)	0.83
Vaginal prolapse	15.7 (24.3)	18 (20.7)	0.65
Vaginal QoL	14.8 (30.5)	18.6 (26.6)	0.56
Sex: urinary	46.2 (31.3)	27.3 (30.8)	<0.05
Sex: bowel	14.3 (25.7)	6 (17.8)	0.13
Sex: vagina	25.7 (33)	23.5 (35.1)	0.79
Dyspareunia	19.4 (26)	10.6 (20.2)	0.13
General sex life	42.6 (33.4)	29.2 (29.2)	0.08
Preoperative urodynamic studies performed (%)	33/40 (83 %)	30/39 (77 %)	0.54
Bladder capacity, ml (SD)	561 (127)	537 (72.4)	0.33
Normal study	1/33	–	
Urodynamic stress incontinence (USI) only	28/33 (85 %)	29/30 (97 %)	0.11
USI with DO/hyposcompliance	4/33 (12 %)	1/30 (3 %)	0.13

ePAQ-PF electronic Personal Assessment Questionnaire–Pelvic Floor, ASA American Society for Anesthesiologists, UI urinary incontinence, BMI body mass index, SD standard deviation, OAB overactive bladder, SUI stress urinary incontinence, QoL quality of life, DO detrusor overactivity

improvement of SUI in women with or without NE was 76 and 93 %, respectively (Fig 1). Logistic regression found that NE was a negative predictor for improvement in symptoms of SUI after TVT ($p = 0.037$). Women without NE were 4.3 times more likely to report cure of SUI following TVT: 60 % reported significant improvement in symptoms of NE after TVT ($p < 0.005$); 24 reported cure of NE, one reported improvement, 13 reported

no change and two reported worsening symptoms. Neither pre-operative symptom profiles nor urodynamic findings were predictive of impact of TVT on symptoms of NE (Table 3).

Improvements in NE were significantly associated with improvement in SUI ($p < 0.005$) were but not related to improvement in OAB ($p = 0.335$) or nocturia ($p = 0.141$). In other words, although symptoms of OAB, SUI and nocturia all showed

Table 3 Impact of transvaginal tape (TVT) on nocturnal enuresis (NE): comparison of symptom profiles and urodynamic findings

	NE improved/cured <i>n</i> = 25 (60 %)	NE no change/worse <i>n</i> = 15 (40 %)	<i>P</i> value
Mean age, years (range)	53 (33–73)	51 (41–69)	0.47
Preoperative SUI domain score, mean (SD)	78 (14)	73 (21)	0.41
Preoperative OAB domain score, mean (SD)	38 (16)	41 (23)	0.65
Preoperative nocturia symptom score (SD)	1.5 (1.2)	1.9 (1.0)	0.32
Preoperative urodynamic studies performed	20/25 (80 %)	13/15 (86 %)	0.59
Bladder capacity, ml (range)	507 (400–600)	490 (315–750)	0.55
Urodynamic stress incontinence (USI)	19/20 (95 %)	12/13 (92 %)	0.75
Preoperative DO or hypocompliance	3/20 (15 %)	1/13 (8 %)	0.53

SD standard deviation, *OAB* overactive bladder, *DO* detrusor overactivity

significant improvement following TVT, only the improvement of SUI was associated with a significant improvement of NE.

Discussion

The primary objective of this study was to investigate the prevalence of NE and its association with other LUTS in women attending a urogynaecology clinic. The main findings are that NE is significantly associated with symptoms of OAB, SUI and nocturia and is reported by approximately one in four women attending urogynaecology clinics. NE is a marker of more severe SUI and OAB in women undergoing TVT and appears to be a negative predictor of successful outcome. However, 76 % report cure or improvement in SUI, and 60 % report cure or improvement in NE postoperatively.

Having self-selected a cohort of patients with a high prevalence of LUTS, we anticipated that prevalence of NE (23 %) would be higher than in the general population (0.5 %) [2]. A study of 12,795 women undergoing urodynamics, which is more comparable with our cohort, reported an NE prevalence rate of 14 % [7]. The higher prevalence in our study may be related to use of the ePAQ-PF questionnaire, which enquires specifically about the symptom of NE as part of a comprehensive assessment of pelvic floor symptoms. The use of such a detailed assessment tool has provided an opportunity to analyse how NE relates to other LUTS in a large cohort of women.

We found NE to be significantly associated with the reporting of symptoms of OAB ($p < 0.005$), a finding supported by Madhu et al. [7]. NE has been associated with DO [6] and DO incontinence [7]. As we investigated symptom profiles in a cohort of women who attended a urogynaecology clinic, we were unable to compare our data with these urodynamic findings.

To our knowledge, our study is the first to report an association between the severity of SUI and NE. Madhu

et al. [7] reported a significant association between NE and low MUCP but no significant relationship between NE and symptomatic SUI or urodynamic stress incontinence. We sought to further explore this finding by analysing a cohort of women undergoing TVT using validated detailed questionnaire data (ePAQ-PF). We found that almost half of women undergoing TVT reported NE preoperatively, of whom 60 % reported improvement or cure postoperatively. Women undergoing TVT who reported NE were significantly more likely to smoke and had significantly higher BMI. These findings are consistent with those reported by Madhu et al. [7] in which high BMI (OR 1.47, $p < 0.001$) and cigarette smoking (OR 2, $p < 0.001$) were significantly associated with SNE. Women undergoing TVT who reported NE had significantly worse lower urinary tract function evidenced by higher symptom scores for SUI, OAB and voiding dysfunction and impact of bladder symptoms on both QoL and sexual function. In women with mixed incontinence undergoing midurethral sling surgery, symptoms of urgency and urge incontinence have been reported to be cured in ~50 % of cases [13]. It might be considered that improvement in symptoms of NE after TVT is secondary to improvement in symptoms of OAB. However, regression analysis confirmed that improvement in NE was only associated with improvement in SUI, not in OAB. This suggests that women with SUI may report symptoms of NE secondary to sphincteric weakness. It follows that in these women, NE may be successfully treated with incontinence surgery: 76 % of women with NE reported successful outcome with respect to improvement in SUI. When compared with women without NE, presence of NE was a negative predictor of successful short-term outcome (76 vs 93 %, $p = 0.037$). We hypothesised that poorer outcome following TVT in women reporting NE may be due to DO, as preoperative OAB symptom scores were significantly higher in women reporting NE. However, preoperative urodynamic findings were similar between the two

groups, with no evidence of increased prevalence of DO or hypocompliance in women who reported NE. We acknowledge that these findings are limited by missing follow-up data in 44 % of women undergoing TVT and by the relatively small number of patients analysed ($n = 84$).

We were able to analyse nocturia separately, as this symptom is not included in the domain score for OAB. We found women who reported nocturia three or more times per night were almost three times more likely to report NE. This is consistent with Madhu et al. [7], who reported higher mean nocturia episodes in women with SNE (OR = 1.38, $p < 0.0001$). An association between nocturia and NE is considered to be linked to a combination of nocturnal polyuria, reduced bladder capacity, and impaired arousal to bladder stimuli; an underlying genetic factor is suspected [14]. Childhood NE has been shown to be a significant risk factor for adult nocturia [15] and nocturnal polyuria syndrome [16]. The underlying pathophysiology is thought to be related to a disorder in the diurnal secretion patterns of arginine vasopressin (AVP), an antidiuretic hormone produced by the posterior pituitary [17].

A limitation of this study is a lack of information on NE onset. PNE is twice as common in boys, and improvement or resolution is more likely in children with milder symptoms. Children who continue to experience PNE beyond the age of 10 years are more likely to experience daytime incontinence [4]. Individuals with PPNE are more likely to suffer from depression, low self-esteem and sleep disturbance and are less likely to reach tertiary education [5]. In a study of 30 patients with PPNE who underwent urodynamic studies, 93 % had DO, 79 % had evidence of functional bladder outflow obstruction and 53 % had bladder capacity < 300 ml [6]. Approximately 80 % of adult women who report NE have SNE, and 20 % have PPNE from childhood [2]. It is likely that the aetiology of NE in adult women differs between SNE and PPNE. For example, prevalence of OAB might be higher in women who report PPNE from childhood, whereas prevalence of SUI might be higher in women with SNE.

In conclusion, this study provides insight into NE, a commonly reported symptom in women attending urogynaecology clinics. We propose that NE may have multiple underlying aetiologies, including OAB, SUI and nocturia. To our knowledge, this is the first study to implicate SUI as an important aetiological factor in NE. This finding may affect how women are counselled regarding outcome of TVT surgery. Future studies that differentiate between women with PPNE and SNE, including both questionnaire data and results of urodynamic studies, will improve our understanding of the different aetiologies of NE in adult women.

Compliance with ethical standards

Conflict of interest Mr Stephen Radley is a Director and shareholder of ePAQ systems limited, an NHS spin-out technology company. The other authors declare they have no conflicts of interest.

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