Pelvic Physical Therapy Distance Journal Club
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Trisha Jenkyns PT, DPT, WCS

Childhood nocturnal enuresis-a marker for pelvic floor disorders and urinary tract symptoms in women?
Othman JA, Akerval S, Molin M et al. Int Urogynecol J 2021; 32:359-365. Doi.org:10.1007/s00192-020-04345-x.

Introduction:
Prior studies have identified an association between CNE and symptoms of urinary frequency, nocturia and urge incontinence as an adult but those studies included parous women. This study includes only nulliparous women...which reduces the confounding factors of childbirth. It is one of four studies that uses the same questionnaire data from a project titled the ‘Swedish Pregnancy, Obesity and Pelvic Floor project in Nulliparous Women’. The other three studies are listed in the references of this article.

Childhood Nocturnal enuresis is defined by The International Children’s Continence Society (ICCS) as both a symptom and a condition of intermittent incontinence that occurs during periods of sleep at the age ≥of 5 years or older, regardless of the absence or presence of lower urinary tract symptoms

• Previously it was wetting in discrete portions while asleep after the age of five. To ensure consistency between the ICCS and the ICS definitions, the ICS has adapted the ICCS definition.

Childhood nocturnal enuresis-bedwetting

• Problem for 5-10% of children below the age of ten years, with a much smaller percent of older children and teenagers as well. It is equally common in all cultures and among all social groups.
• Boys are somewhat more often affected than girls, but this gender difference diminishes with age.
• Kids often grow out of it. The condition mostly resolves spontaneously up to the age of 16–17 years, except for a small percentage (0.5-1.7%)
• If CNE is still present at the age of 7 years, the child has a 5–10% risk of having persistent symptoms in adulthood
• Probable genetic component demonstrated by Twin studies, although 1/3rd of cases is thought to be influenced by environmental factors

Causes of CNE

• Difficult to arouse from sleep at night, they may have nocturnal polyuria, or reduced bladder capacity
• It is often associated with daytime UI, bowel dysfunction- particularly constipation, as well as developmental or psychological problems. Stress is also thought to be a big component.

First-line treatments with proven effect are the enuresis alarm (sound signal occurs when bed is wet and can gradually helps child to recognize the body’s own signals) and the other first line treatment is the drug desmopressin (Minirin-reduces the amount of urine produced by the kidneys at night). Approximately 75% of all bedwetting children become dry by these methods.

Aim/Primary Aim: Describe the prevalence of pelvic floor disorders and LUT symptoms in nulliparous women, with or without history of CNE which occurred at 5 years old or older.

Study Design/Study Format: Observational prospective cohort study. Age groups were stratified into decades to help predict population trends

Subjects were from Sweden’s registry called the Total Population Register (TPR) where data is collected for research and statistical purposes.
The registry keeps data on their residents, including name, place of residence, gender, age, civil status, place of birth, citizenship, immigration, biological and adopted children, etc., and is updated every 6th week.

There were 625,810 eligible nulliparous women in this registry. 20,000 nulliparous women between the ages of 25-64, were randomly selected from this group of registered women to participate in their study. The upper age limit of 65 was used to decrease the influence of potential confounding age-dependent comorbidities.

This group was stratified by 4 decades starting 25–34, 35-44, etc. up to 64 years and questionnaires were sent out. A little more than half returned the questionnaire, and this group was pared down to 9197 because of missing information, their answers revealed pregnancy and parity, or women declined to participate.

Methods:
This group of women answered a survey with 40 questions, including questions about height, weight, menstrual status, pregnancy, hormone treatment, hysterectomy, childhood enuresis as well as UI, FI, POP, nocturia, urgency.

Questions were divided into ‘symptoms from urinary tract’ (SUI, UUI & MUI, OAB), “symptoms from the vagina” (POP), and “symptoms from the back passage” (FI), and if these symptoms were present how much they were bothered or affected by them. The amount and frequency of leakage was also asked.

UI was defined by the question “Do you have involuntary loss of urine?” Participants reporting UI were also asked if the incontinence had been present for > 10 years.

Nocturia was determine if voiding occurred ≥ 2 times/night

CNE was determined with these questions... “Were you a bedwetter during childhood? If yes, when did it stop?”

The actual survey from this Swedish Project is included as an appendix in the first study. (Othman 2017)

Statistical Analysis: Student’s T test was used when comparing continuous variables and the Fishers exact test for categorical variables. Differences between groups was analyzed using a logistic regression model and presented as adjusted odds ratios. The trend between age groups was analyzed with Mantel-Haenszel statistics.

Results:
Table 1: You will find some of their significant findings when comparing the 926 women reporting CNE & the 8140 that reported no CNE. There were 131 women that did not answer the question about CNE. (98.6% did). Significant findings (p value of <0.0001) of the 926 women reporting CNE tended to be:

- Younger (somewhat-2.1 years), less often postmenopausal, and mother had UI.

Table S1 (supplementary): Displays that CNE was more present in younger group of women (25-34 y.o.) than the oldest group (55-64 y.o.)

- The authors acknowledge this as a recall bias, as older women may have forgotten. This higher prevalence may also because younger women are less concerned of any stigma admitting CNE.

Table S2: Displays comparisons between different age groups and the finding that each age group reported similar association between PFD’s and CNE.

Table 2: Comparisons between the CNE group and non-CNE group and their answers on pelvic floor disorders. There were several significant findings (p values <0.0001)

1. Main finding: prevalence of UI and all subtypes (UUI, SUI, MUI), was doubled or almost doubled in women with CNE, including OAB and moderate to severe UI. The strongest association was for MUI.

2. Daytime micturition ≥ 8x and nocturia ≥ 2X were significantly higher in CNE group
3. CNE group was more likely to have more than 1 PFD
4. Interestingly, POP and FI were also consistently higher in CNE group
   - Authors stated some skepticism about the high number of nulliparous women with POP symptoms and contemplated that the bulging question may have produced false positive responses. They still conclude that the difference in prevalence between women with and without CNE reflects a real difference in pelvic support.

**Discussion:**
This study shows that CNE was a significant predictor of several PFD’s. The authors see this as an indication that there may be at least one common causal factor linking CNE to these adult PFD’s but they do not state any causal factors

**Strengths:**
- The major strength was Including only nulliparous women therefore by eliminating confounding factors of pregnancy & childbirth. Other studies that looked at the link between CNE and adult PFDs included women with mixed parity, so the results were conflicting.
- The 11.4% rate of CNE found in this study closely matches the 10.8% rate from a cited meta-analysis of 15 different studies.
- It was a large study. Sample of participants was randomly selected from a very large Swedish registry.
- Limiting the age span of 25 to 64 years helped to remove the confounding effects of elderly illnesses and the tendency for UI to worsen with age.

**Weaknesses:**
- Surveys are chosen because they are relatively easy and inexpensive but with no objective confirmation, we must trust the respondent is providing accurate and honest answers resulting in a confounding bias
  - Respondents may not feel comfortable providing answers about their bowel & bladder habits
  - Common for many people to not recall the actual number of times they void or leak per day or night!
- Data errors may be caused by who does and doesn’t respond to the invite or answer a questionnaire. The number of respondents who choose to respond to a survey question or questionnaire may be different from those who chose not to respond, thus creating bias.
  - The authors looked at the demographics of nonresponders vs. responders, and found the nonresponders were younger, more often immigrants (non-Swedish citizens), less often married, lower income, lower education.
  - A lower socioeconomic status is known to be associated with predictors of UI, so we might have seen different results because of who answers a questionnaire

**Clinical Application**
- How can we use these findings to help our clients?
- Would knowing this potential connection, and the study results be helpful information for our clients?
- The findings of this study reinforce the importance of parents learning and practicing healthy bladder and bowel habits, so they can support healthy habits for their children.
- This study also lends support to the overall importance of bladder education and prevention.
- Any ideas for future research?

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1 Al-Mukhtar Othman, J., Akervall, S., Milsom, I., Gyhagen, M. (2017). Urinary incontinence in nulliparous women aged 25-64 years: a national survey. American Journal of Obstetrics & Gynecology, 216, 149.e1-149.e11.