

Start	End	Topic	Speakers
10.30	10.50	Nocturia in relation to Menopause	Wendy Bower
10.50	11.10	Nocturia and Cardiovascular Causalities	Kari Tikkinen
11.10	11.30	Understanding the Effect of Fluid Intake on Diuresis and Water Balance	Karel Everaert
11.30	11.50	Understanding the Effect of Food on Diuresis.	François Hervé
11.50	12.00	Discussion	François Hervé Wendy Bower Kari Tikkinen Karel Everaert

### **Aims of Workshop**

The general aim of this workshop is to contribute to the existing knowledge of Nocturia, with a special focus on its multidisciplinary aspect.

It stresses the collaboration and teamwork that is needed to integrate knowledge through cross-disciplinary talks.

It seeks to improve management of nocturia by translating fundamental scientific discoveries and critically evaluated clinical observations into practical clinical applications, bridging good science with good practice.

### **Learning Objectives**

Improve our knowledge by understanding some mechanisms of action or underlying physiopathology involved in Nocturia

### **Target Audience**

Urology, Urogynaecology and Female & Functional Urology, Conservative Management

### **Advanced/Basic**

Intermediate

### **Suggested Learning before Workshop Attendance**

International Continence Society consensus on the diagnosis and treatment of nocturia

Neurourol Urodyn. Feb;38(2):478-498. PMID: 30779378

How can we develop a more clinically useful and robust algorithm for diagnosing and treating nocturia? ICI-RS 2017

Neurourol Urodyn. 2018 Jun;37(S4):S46-S59 PMID: 30133785

**Wendy BOWER, PhD, Dip epi Biostats, BAppSc**

**Physiotherapist**

**Australia**

Approximately 40% of women older than 40 years report nocturia without other urinary tract symptoms. Nocturia in women after midlife has a mixed pathophysiology and cannot be considered solely a feature of the overactive bladder nor as only resulting from high fluid intake or diuresis rate at night. Nocturia has been reported more often in the presence of hot flushes (38% compared with 32%) (OR 1.49, 95% CI 1.19-1.87) and also in women after a hysterectomy (53% compared with 33%) (OR 1.78, 95% CI 1.08-2.94).

Nocturia is sensitive to hormone replacement: significant reduction in nocturia prevalence after 6 months of HT from 27.7% (59/213) to 16.4% (35/213). Nocturia frequency unchanged in 67.7% (65/96) of women after 6 months of hormone therapy. (Pauwaert K et al 2020)

Factors related to nocturia  $\geq 2$  in women at midlife:

- age (OR 1.04, p=0.038)
- vitamin D supplementation (OR 2.33, p=0.026).
- night sweating (OR 2.25, p=0.052)
- flushes during the day (OR 2.67, p=0.025)
- regular exercise (OR 0.38, p=0.012).

Nocturia unaffected by intake of phyto-oestrogen food, overweight status, urogenital prolapse, loss of sexual interest or vaginal dryness. Bladder diary measures unchanged by use of probiotics, non-steroidal anti-inflammatory medications, vaginal oestrogen or the presence of night sweating.

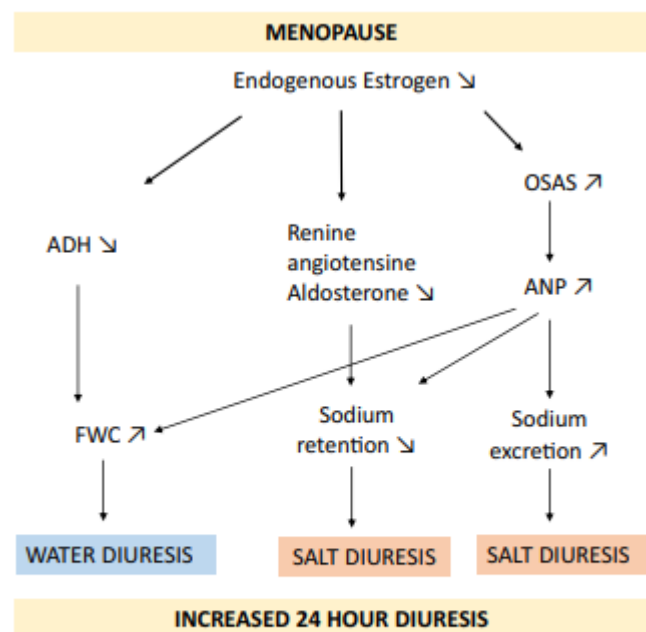
Each of the physiological mechanisms underlying nocturia are impacted by menopause:

Reduced bladder capacity: oestrogen receptors in vulva, vagina, bladder trigone, proximal and distal urethra

- Maximum voided volumes significantly lower after menopause: possible 50% decrease
- Nocturia  $\geq 2$  compared to other women (Night: 268ml vs 350mL,  $p=0.006$ ; Day: 200mL vs 290mL,  $p<0.001$ ).
- OAB: Urinary urgency (OR 3.97 95% CI 1.7-9.26)
- NBCi > 1.3 observed in 26.2% women > 40 years
- Associated with day flushes
- Estrogen only treatment can significantly reduce urgency prevalence (Baseline 36.2 % (17/47), after treatment 19.1% (9/47),  $p = 0.039$ ).

### Nocturnal polyuria

From: Pauwaert K et al. International Urogynecology Journal. 2021 Jan 13:1-0.



**Fig. 2** Potential endocrinological mechanisms in postmenopausal women. *ADH* antidiuretic hormone, *ANP* atrial natriuretic peptide, *FWC* free water clearance, *OSAS* obstructive sleep apnea syndrome

- Excessive night urine volume (nocturia index > 1.3) 77.7 % of women at midlife
- 45% increase in nocturnal bladder capacity index in women reporting daytime flushing
- 64.6% of women > 40 years studied; seen in 78.1% of women with nocturia  $\geq 2$
- Predicted by: i) Age (OR 1.06, CI 1.026-1.105; ii) Flushes by day (OR 2.96, CI 1.250-7.029)
- Protective factors; iii) 150 minutes of exercise per week – OR 0.30, 95% CI 0.134-0.638 and iv) use of HRT – OR 0.18, 95% CI 0.032-0.990.

### Impaired sleep

- Insomnia: sleep onset latency (OR 2.25 95% CI 1.03-4.92) (Pauwaert K et al 2021)
- Insomnia: difficulty returning to sleep (OR 3.99 95% CI 1.58-9.61) (Pauwaert K et al 2021)
- Short FUST
- Short overall sleep time
- Poor quality sleep
- Thermoregulation changes: night sweating
- Menopause is a risk factor for sleep apnoea: associated with increase in nocturnal diuresis due to sodium excretion
- Obesity, GORD, thyroid dysfunction chronic pain, fibromyalgia all increase prevalence around menopause
- Significant reduction in SLEEP sumscore on TANGO after hormone therapy: decrease from 8.5 (5.1-11.5) to 5 (0.0 – 8.4) ( $p < 0.001$ ).

**Kari TIKKINEN MD, PhD**  
**Urologist**  
**Finland**

**To be completed**

**Karel EVERAERT, MD, PhD**  
**Urologist**  
**Belgium**

Standard therapy of nocturia starts with lifestyle interventions as decreasing fluid intake although this advice is put forward with limited evidence. There is no more than level 2 evidence that modifying fluid intake is helpful for urinary incontinence and especially for nocturia. The aim of this lecture is to discuss the evidence and the complexity of performing future research in this field.

The effect of fluid intake on nocturnal urine output and nocturia not only depends on the amount of fluid but also the type of fluid and is indirectly related to conservative measures like weight loss, physical activity, constipation. Intake of fluid is connected with intake of foods and both might have an effect on the bladder or the urine output meaning that one really has to modify 1 aspect of intake and study the effects on bladder, kidney and sleep!

The impact on the circadian rhythm has to be studied accordingly and we need to study the time-delay by intake and effect on the bladder, kidney or sleep. It might be that in example limiting fluid intake in the morning or during the day is more relevant than in the evening. The time delay between intake and effect also depends on food intake and composition as moisture, macronutrients, electrolytes, presence of diuresis promoting agents as alcohol, caffeine or other bioactive phytochemicals (studied in animal studies), and might be different during the day or the night or different between persons with or without nocturia.

Modifying fluid intake must be considered as behavioral therapy and its multiple mechanisms of action making it really difficult to study the effect of water and only water in individuals with nocturia. Just the effect of adding a intake and or voiding diary might change the behavior of a patient significantly. Also cognitive behavioral therapy might influence not only urine output but as well the bladder function as the sleep and indirectly improve nocturia.

The effect of nutrition and fluid intake on sleep might influence nocturia. The best-known examples are alcohol and caffeine however many nutrients are important in the synthesis of endogenous melatonin which might also influence sleep. This is however barely studied.

Many liquids and foods might have a different impact depending on dose, gender, age, food composition, meal timing, habitual intake and individual variations in responding, easily illustrated by the many conflicting studies of the effect of alcohol on LUTS in general.

When studying the effect of fluid intake on nocturnal urine output, studies must be performed with well specified types of fluid, standardizing intake of foods, measuring urine output at night in a nocturia population without neglecting the different component of nocturia (bladder, sleep and kidney).

**François HERVÉ, MD, PhD**  
**Urologist**  
**Belgium**

When addressing the treatment of Nocturia, it is recommended to start with non-invasive measurements and lifestyle advices. Reducing fluid intake in the evening is of common sense. But next to fluid intake, food and other nutrients have also to be considered.

Urine is produced in order to regulate the body fluid homeostasis, electrolytes, the acid–base balance and to remove toxins and by-products.

Foods may participate for up to 20% of total daily fluid intake in the form of water in food.

Also, specific compounds in foods may also have a direct diuretic effect.

Fluid, salt and food intake may increase diuresis rate and may alter the circadian rhythm of urine production: food and beverages which are the main dietary source of fluids, electrolytes (for example, sodium, potassium, or calcium), and other osmotically active substances (for example, urea and glucose) can therefore promote diuresis.

Alwis and al.(1) have conducted a systematic review about the impact of food and drinks on urine production.

High dietary sodium, as well as wine, spirits, and high-caffeine coffee, caffeinated energy drinks, increased UV in human studies.

Consuming meat meal (beef) compared with an equivalent amount of sodium and water, significantly increased urinary sodium excretion, but not urine flow in healthy men. Understanding the effect of food on diuresis is important in non-pharmacological management and first line treatment of many clinical conditions, particularly nocturia and polyuria. Unfortunately, the precise physiological relationship between foods/food constituents and renal water elimination in humans remains poorly defined.

Food can have an impact on voiding complaints by its indirect effect on bladder and prostate, reducing the inflammatory process. For example, antioxidant phytochemicals that are found in fruits and vegetables reduce inflammation. Healthy food can have an impact on reducing hyperglycemia and consequently decrease oxidative stress and inflammation. It may have a beneficial effect on nocturia, particularly in the setting of overactive bladder, bladder outlet obstruction secondary to benign prostatic hypertrophy, and other urinary storage symptoms, which are important contributors to nocturia that are often related to an inflammatory process. Notably, intake of vegetables, fruits, vegetable fats, citrus juice, pumpkin seeds, bread, chicken, dietary isoflavone, and beer and intake levels of vitamin D, protein, and potassium demonstrated significant negative associations with OAB and BPH.

Finally, another aspect needs to be considered: the relationship between foods and diuresis may be indirectly mediated by melatonin. Melatonin is a neurotransmitter hormone that is critical for sleep maintenance and the regulation of circadian rhythm. Intake of cereals, vegetables, fruits, caffeine, and certain vitamins and minerals may modify melatonin production in the body.

1. Alwis US, Haddad R, Monaghan TF, Abrams P, Dmochowski R, Bower W, et al. Impact of food and drinks on urine production: A systematic review. *Int J Clin Pract* [Internet]. 2020 Sep [cited 2021 Sep 11];74(9):e13539. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/32441853>