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**Định nghĩa tiêu đêm**

- Nocturia defined by International Continence Society (ICS) as:  
" \_\_\_\_\_ "
- Than phiền BN phải thức dậy  $\geq 1$  lần để đi tiểu.
- Cảm giác muốn tiểu đánh thức BN dậy để đi tiểu  
\_\_\_\_\_ "

van Kerrebroeck et al. 2002

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**Bệnh cảnh cần phân biệt**

- Tiêu đêm  $\neq$  Tiêu dầm(không thức dậy đi tiểu)
- Tiêu dầm  $\rightarrow$  không ý thức  $\rightarrow$  ướt đồ lót.

! Khó ngủ  $\rightarrow$  thức dậy thường xuyên  $\rightarrow$  đi tiểu mỗi khi thức dậy

! Uống nước sau đi tiểu  $\rightarrow$  đi tiểu  $\rightarrow$  uống nước  $\rightarrow$  đi tiểu.....

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**What triggers nocturia?**

- 50 men and women
  - Mean number of nocturia events = 2.6
- Nocturia awakenings attributed to urge or not?<sup>1</sup>
  - 78% nocturic voids were preceded by urge to void
  - In the remainder, the patient awakened for some other reason, then voided out of habit or convenience before going back to sleep

The aetiology and treatment of these two groups is likely to be different

1. Blavias et al. SUFU abstract 2010

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**Tiểu đêm**

- Ngày càng thường gặp trong quá trình lão hóa:
  - ↓ ADH theo tuổi
  - BQ giảm dung tích theo tuổi
  - Bệnh lý nội/ngoại khoa ảnh hưởng/BQ, thận
- Nguyên nhân thường gặp nhất gây mất ngủ, đặc biệt người lớn tuổi

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**Tiểu đêm**

- Nearly two-thirds (65%) of those responding to NSF's 2003 *Sleep in America* poll of adults between the ages of 55 and 84 reported this disturbance at least a few nights per week. or more (53% every or almost every night).

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# Tiểu đêm

## 50-59 tuổi:

- Nam: 58%
- Nữ: 66%

## > 80 tuổi

- Nam: 72%
- Nữ: 91%

Laureanno P et al(2010). Urol Nurs

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## Nocturia: prevalence (≥2 voids/night)

- Meta-analysis of 43 studies

Gender (age range)	Prevalence
Men (20–40 years)	2–17%
Women (20–40 years)	4–18%
Men (>70 years)	29–59%
Women (>70 years)	28–62%

Borch & Weiss. J Urol 2010;184:440–446

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## Study: Nocturia Common Among Japanese Patients

Medwire (12/2, Oswald) reports that research published online in Lower Urinary Tract Symptoms indicates that **“nocturia is common among Japanese patients, with men, the elderly, and those with hypertension at the greatest risk.”** Investigators “say that the majority of previous studies into nocturia prevalence have come from referral-based samples and therefore had limited generalizability to the overall population

AUA News Dec 2013

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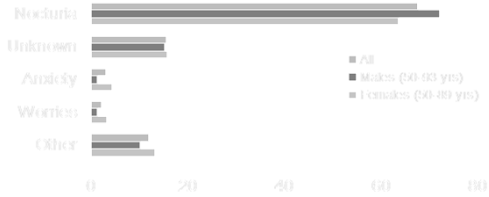
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### Nocturia: the most common cause of sleep disturbance in over 50s

Prevalence (%) of main causes of disturbed sleep maintenance in individuals aged 50-93 (n=1117) <sup>1</sup>



On average, nocturia patients sleep for an initial period of only 2-3 hours before being awoken by need to void;<sup>2</sup>

1. Middelkoop et al. *J Gerontol A Biol Sci Med Sci* 1996;51:M108-M115; 2. van Kerrebroeck et al. *Eur Urol* 2007;52:221-229

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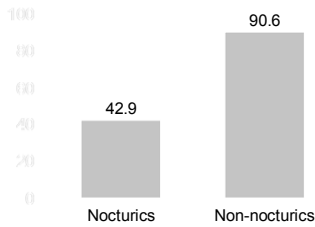
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### LUTS patients have poorer self-rated QoL if they have nocturia

Proportion of patients with LUTS rating QoL as good or very good



LUTS, lower urinary tract symptoms; QoL, quality of life. Hernandez et al. *Curr Med Res Opin* 2008 [Epub ahead of print]

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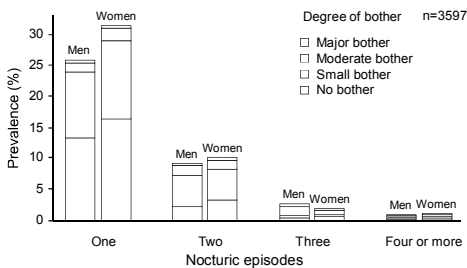
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### QoL in nocturia: bother can be major even with one void/night



Tikka et al. Presented at AUA 17-22 May 2008, Orlando, USA

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**CÁC TÁC ĐỘNG KHÁC CỦA TIỂU ĐÊM**

- Vọp bẻ, chàm chít, kiến bò ở chân, đổ mồ hôi đêm tăng song song với số lần đi tiểu
- Tăng nguy cơ té ngã 2 lần nếu tiểu đêm  $\geq 2$  lần(1)
- Tăng tỷ lệ tử vong(2) .
  - N/c 6.000 người  $\geq 65$  tuổi ở Thụy điển:
    - 190 nam và 287 nữ ghi nhận tiểu đêm  $\geq 3$  lần.
    - 44 † ở nam tiểu đêm  $\geq 3$  lần và 34 † ở nữ.
    - Tỷ lệ † tăng gấp đôi ở cả nam lẫn nữ tiểu đêm  $\geq 3$  lần
- Ảnh hưởng chức năng miễn dịch(3)

1. Stewart, R.B et al. (1992).. *Journal of the American Geriatric Society*,  
 2. Benca, R.M., & Quintas, J. (1997). *Sleep*,  
 3. Asplund, R. (1999). *British Journal of Urology International*

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**Nguyên nhân tiểu đêm?**

**NGUYÊN NHÂN DO BÀNG QUANG**

- Bể tất BQ: Bướu TLT, hẹp niệu đạo...
- BQ tăng hoạt
- Nhiễm trùng niệu
- Viêm BQ
- Viêm mô kẽ BQ
- Bướu BQ
- Xạ trị
- Rối loạn cơ vòng- BQ thần kinh- Sa bàng quang

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**Nguyên nhân tiểu đêm?**

**NGUYÊN NHÂN KHÔNG LIÊN QUAN ĐẾN BQ**

- Tăng huyết áp, Suy tim sung huyết
- Phù chi dưới ứ trệ máu tĩnh mạch ngoại vi( peripheral venous stasis),
- Ngưng thở lúc ngủ
- Rối loạn giấc ngủ
- Bệnh thận mạn, suy gan
- Dược chất: diuretics, cardiac glycosides, demeclocycline, lithium, methoxyflurane, phenytoin, propoxyphene, thừa vitamin D
- Uống quá nhiều trước khi ngủ: đặc biệt là cà phê, sản phẩm chứa caffein, rượu bia.

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**Nguyên nhân tiểu đêm?**

**NGUYÊN NHÂN KHÔNG LIÊN QUAN ĐẾN BQ**

- Đái tháo đường không điều trị (Type 1 và Type 2)
- Đái tháo đường do thai kỳ
- Đái tháo nhạt
- Giảm tiết ADH

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**Nguyên nhân tiểu đêm?**

**NGUYÊN NHÂN TIỂU ĐÊM HỖN HỢP**

Các nguyên nhân trên trong bệnh cảnh vừa đa niệu về đêm vừa giảm dung tích BQ

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**Bệnh cảnh lâm sàng**

- Đa niệu (polyuria): Lượng nước tiểu nhiều (> 2 lít/ngày)
  - Đa niệu về đêm (nocturnal polyuria):  
Lượng nước tiểu nhiều về đêm: : ↓ADH  
+++ : thường gặp nhất
  - Tiểu đêm hỗn hợp (mixed nocturia): Đa niệu về đêm + giảm dung tích BQ
- ⇒ Nhiều nước tiểu sản xuất về đêm vượt quá dung tích BQ → buồn tiểu → bị đánh thức để đi tiểu

↓  
**MẤT NGỦ**

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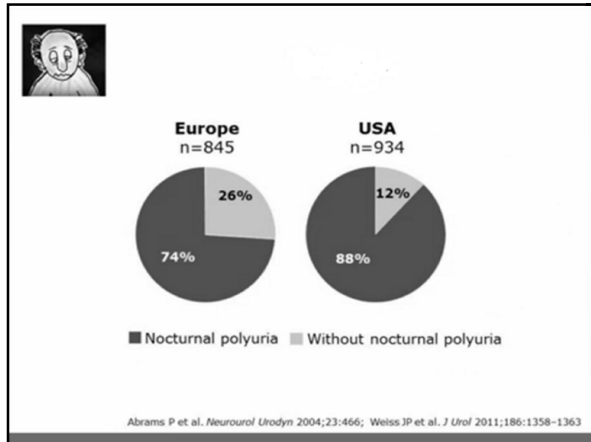
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### ĐA NIỆU VỀ ĐÊM

- Sản xuất nước tiểu nhiều một cách bất thường về đêm
- Tổng lượng nước tiểu về đêm:
  - Người trẻ: >20% / tổng lượng nước tiểu 24h
  - Người lớn tuổi: >33% / tổng lượng nước tiểu 24h



van Kerrebroeck et al. NeuroUrol Urodyn 2002;21:179-183

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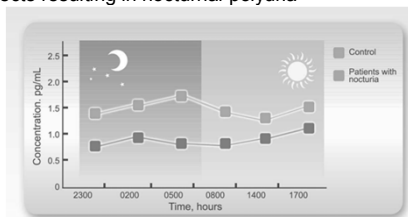
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### Nocturnal Polyuria?

- Nocturia patients secrete less ADH at night than healthy subjects resulting in nocturnal polyuria



Miller, M.: Nocturnal polyuria in older people: pathophysiology and clinical implications. J Am Geriatrics Soc, 48: 1321, 2000. Asplund, R.: The nocturnal polyuria syndrom (NPS). Gen Pharmacol, 26: 1203, 1995.

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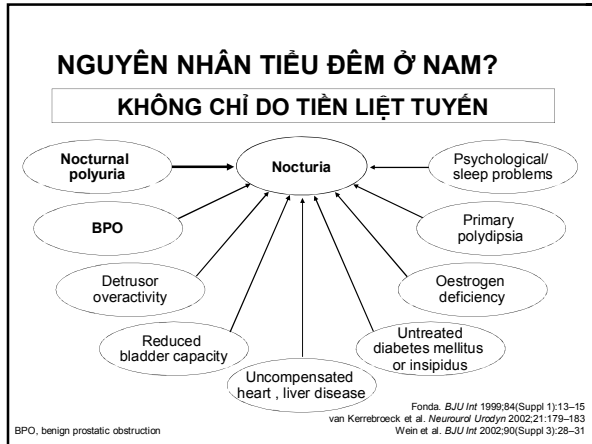
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### Thinking beyond the prostate

- Nocturia in men traditionally regarded as due to detrusor overactivity or bladder outlet obstruction (BOO) – caused by BPO
- However, ~83% of male nocturia patients have nocturnal polyuria (NP)

Causes of male nocturia (total n=41)	Patients (%)
<b>Single isolated causes</b>	
NP	8 (19.51)
Small nocturnal bladder capacity	2 (4.88)
BOO	1 (2.44)
Sleep apnoea syndrome	0 (0)
<b>Double combinations</b>	
NP + small nocturnal bladder capacity	6 (14.63)
NP + BOO	8 (19.51)
Small nocturnal bladder capacity + BOO	4 (9.76)
<b>Triple combinations</b>	
NP + small nocturnal bladder capacity + BOO	10 (24.39)
NP + small nocturnal bladder capacity + sleep apnoea syndrome	2 (4.88)

Chang et al. *J Urol* 2006;67:541-544

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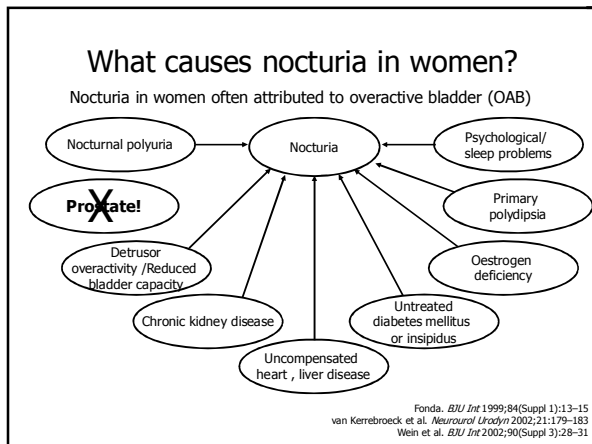
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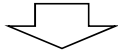
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**ĐIỀU TRỊ TIỂU ĐÊM**

•••• Điều trị tùy thuộc loại và nguyên nhân

•••• Các lựa chọn:



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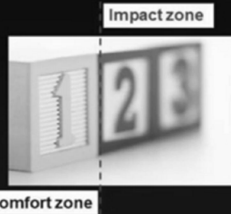
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**What degree of nocturia is important?**

- Results from multiple studies of mortality, fractures and QoL all show  $\geq 2$  voids/night is a 'threshold' for significant negative impact from nocturia
- One void/night is less likely to have serious consequences
- If treatment can reduce nocturia frequency to  $< 2$  voids/night on average, risks and bother to patients may be significantly reduced



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**ĐIỀU TRỊ TIỂU ĐÊM**

**Can thiệp:**

- Giảm lượng nước nhập về tối (nhất là: cà phê, sản phẩm chứa cà phê, rượu bia)
- Thời gian dùng thuốc lợi tiểu (giữa buổi chiều, 6h trước khi đi ngủ).
- Ngủ trưa.
- Nâng cao chân.
- Mang vớ bó chân.

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**ĐIỀU TRỊ TIỂU ĐÊM**

**Thuốc:**

- Kháng cholinergic: ↓ triệu chứng BQ tăng hoạt
- Bumetanide (Bumex), Furosemide (Lasix): điều hòa sản xuất nước tiểu
- Imipramine (Tofranil): giảm sản xuất nước tiểu
- **Desmopressin (DDAVP): giúp thận giảm sản xuất nước tiểu**

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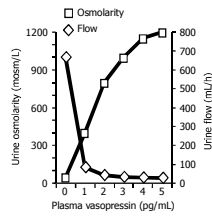
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**Desmopressin: Treatment for nocturia**

- Desmopressin - Synthetic analogue of antidiuretic hormone arginine vasopressin (AVP)
- No effect on V<sub>1</sub> receptors
- Greater effect on renal V<sub>2</sub> receptors than vasopressin
- Avoids undesirable vasopressor and uterotonic effects
- **Increases reabsorption of water, concentrating urine and decreasing urine production**



Nergaard et al. *NeuroUrol Urodyn* 2007;00:1-8  
Adapted from Figure 1, page 8 of Robertson and Nergaard. *BDU Int* 2002;30:7-10 with permission of Blackwell Publishing Ltd.

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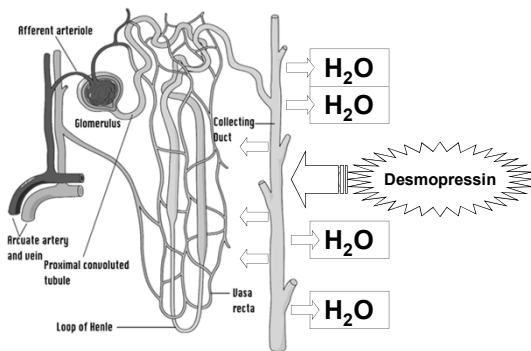
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**Desmopressin (MINIRIN®)**




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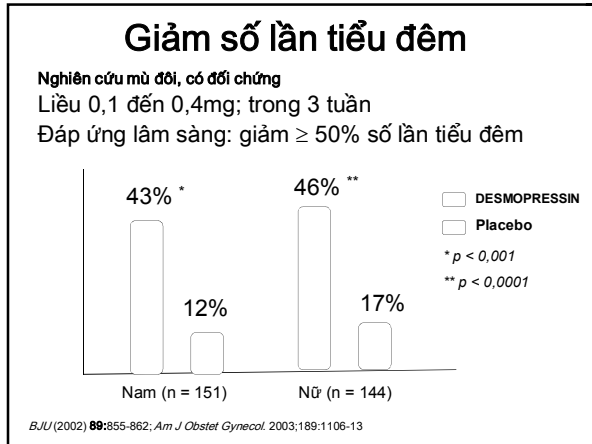
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- Sleep is vital for:  
**Health** **Well-being** **Alertness** **Essential biological/physiological rhythms**
- Fragmented sleep can impair all of these
- Nocturia is the major cause of fragmented sleep and therefore has many non-trivial consequences
- Nocturia should be treated to bring meaningful benefits for the patient

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### The time of awakening is important for daytime functioning

- Awakening from REM sleep is most natural moment for arousal
- Waking up during the first 3–4 hours of the night (SWS) is more likely to leave a person groggy and tired during the following day than waking up later at night

...and remember, every time a person awakes, it is probable that their partner is woken too...

Stanley. European Urology Supplements 2005;3:17-23

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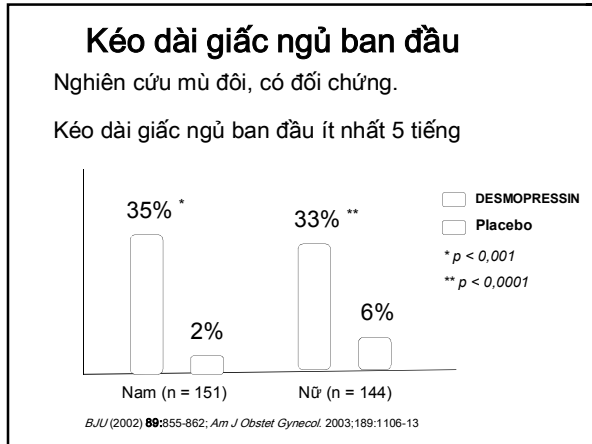
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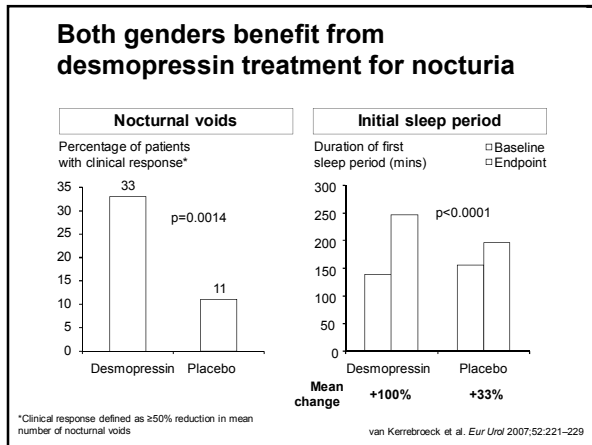
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### Symptom bother is reduced with long-term treatment

Time	Percentage of women
Baseline	79
Long-term study start	68
10 months	30
12 months	31

Proportion of patients with nocturia as most bothersome symptom decreased by  $>50\%$  during long-term treatment

Lose et al. *J Urol* 2004;172:1021-1025

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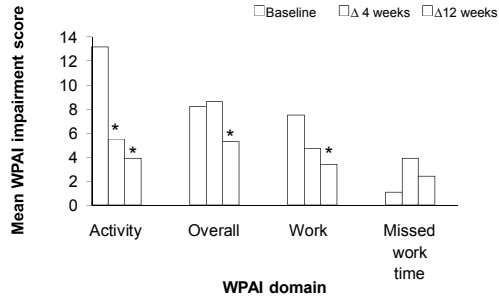
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### Work productivity is improved with desmopressin treatment



\*p<0.05  
WPAI, work productivity and activity impairment  
Holm-Larsen et al. Presented at AUA, May 17-22 2008, Orlando, USA; abstract 158

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### Combination therapy may also be used for patients with nocturnal polyuria

- Combination therapy should also take NP into account to alleviate nocturia
- Patients may have:
  - BPO + NP
  - OAB + NP
  - BPO + OAB + NP
- Therefore:
 

antimuscarinic

 ⊕ 

α<sub>1</sub>-blocker

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desmopressin

may be required for successful nocturia treatment
- Clinical studies to evaluate benefits of combination therapy are warranted

NP, nocturnal polyuria; BPO, benign prostatic obstruction; OAB, overactive bladder

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### Nocturia needs to be treated according to its causes

- If a patient has nocturia and diagnosis of OAB or BPO, they may ALSO have NP
- If NP present, consider combination therapy:

Diagnosis	Desmopressin	Anticholinergic	α <sub>1</sub> -blocker
NP	✓		
OAB		✓	
BPO			✓
NP + OAB	✓	✓	
NP + BPO	✓		✓
OAB + BPO		✓	✓
NP + OAB + BPO	✓	✓	✓

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**Desmopressin and oxybutynin in monosymptomatic nocturnal enuresis: a randomized, double-blind, placebo-controlled trial and an assessment of predictive factors**

- BN: 206 trẻ em 6- 13 (trung bình 10.6 ± 2.9 tuổi), 117 nam bị tiểu dầm về đêm.
- Điều trị kết hợp Desmopressin + Oxybutynin/đơn trị
- Kết quả: Điều trị kết hợp hiệu quả trong điều trị tiểu dầm về đêm (MNE; 45% thành công so với 17% giả dược; OR, 0.24; 95% CI, 0.10 - 0.56; P < .01),, đặc biệt hiệu quả khi có giảm dung tích BQ và thành BQ dày

Montaldo, P., et al(2011). *BJU International*.

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**AUA ANNUAL MEETING**  
MAY 4 - 8, 2013  
SAN DIEGO, CA, USA

SHARING KNOWLEDGE.  
SETTING STANDARDS.

**NOCTURIA**

Maeda et al (1951), "Obstructive Sleep Apnea Syndrome (OSAS) Should be Considered as One of the Causes for Nocturia in Younger Patients without Other Voiding Symptoms."

- The severity of OSAS correlated w/ worsening nocturia.
- CPAP reduced # awakenings up to 90%.
- Nocturia in men <50y w/ other voiding symptoms is diagnostic of OSAS.

Dmochowski et al (1953), "Treatment of Nocturia in Women: Results of Randomized, Controlled, Double-Blind 3-month, Phase III Safety and Efficacy Study of Desmopressin Orally Disintegrating Tablet."

- A randomized, controlled, double-blind multi-institutional 3 mo study confirmed the efficacy of 25mcg of desmopressin for female nocturia w/ significant hyponatremia.

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**Effect of Desmopressin with Anticholinergics in Female Patients with Overactive Bladder**

- Purpose: evaluate the effect of desmopressin combined with anticholinergics on daytime frequency and urgency in female patients with overactive bladder (OAB)
- Materials and Methods:
  - 68 female patients with OAB.
  - Randomly assigned: Treatment 2w
    - group I: 5 mg solifenacin
    - group II: 5 mg solifenacin + 0.2 mg desmopressin.
  - Assess changes in voiding symptoms and QoL
  - A pre/post-treatment 3-day voiding diary
  - Urinary Distress Inventory (UDI-6) + Incontinence Impact Questionnaire (IIQ-7)

Young Kook Han et al. *Korean J Urol*. 2011

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**TABLE 1**

Baseline patient characteristics in each group (mean±SD)

Click on image to enlarge			
	Group I	Group II	p-value
No. of patients	31	37	
Age (yr)	56.3±6.7	52.3±8.1	0.107
Time to first void (min)	78±12.3	82±18.7	0.172
Time to first urgency episode (min)	196±32.5	187±27.7	0.182
No. of voids (first 8-hr)	5.1±1.2	4.8±0.8	0.327
No. of urgency episodes (first 8-hr)	2.8±0.4	3.2±0.4	0.572
UDI-6	43.1±22.6	48.7±17.3	0.272
IIQ-7	48.8±26.8	52.3±18.2	0.731

UDI-6: Urogenital Distress Inventory, IIQ-7: Incontinence Impact Questionnaire

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**Effect of Desmopressin with Anticholinergics in Female Patients with Overactive Bladder**

	GROUP I(GI)	GROUP II(G II)	GI - GII	p
N	31	37		
First void	102 min	117 min	- 12min	NS
Second void	203 min	255 min	- 52min	Significant
Third void	312 min	368 min	- 56 min	Significant
First urgency episode	212 min	255 min	- 43 min	Significant
QoL score*	Significant Improvement	Less Improvement		

\*: ↑ time to 1<sup>st</sup> void >10% → G II effective > G I (pts > 65y, w/ Vu > 150ml)

**Conclusion:** Desmopressin combined with anticholinergics more effective than anticholinergics only in the treatment of female patients with OAB.

Young Kook Han et al. Korean J Urol. 2011

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**Desmopressin May Reduce Nocturia In Men With Late-Onset Hypogonadism**

Renal and Urology News (9/24, Frei) reports that research presented at the 33rd Congress of the Société Internationale d'Urologie suggests that "desmopressin treatment appears to reduce nocturia and other lower urinary tract symptoms while also significantly increasing testosterone levels in men with late-onset hypogonadism." The findings, "from a 62-patient prospective trial, suggest that nocturia may be related to hypogonadism in this population

AUA News Sept 2013

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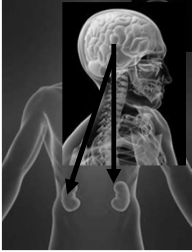
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### Conclusions

#### Think beyond the bladder – to the kidneys!



- >80% TĐ có ĐNVD
- Cần chú ý BLTLT hay H/C BQ tăng hoạt kết hợp với ĐNVD
- Desmopressin điều trị hiệu quả TĐ do ĐNVD
- Điều trị kết hợp đang là chuẩn mực nổi lên
- Desmopressin có thể kết hợp với anticholinergics +  $\alpha_1$ -blockers để cải thiện TĐ nơi BN BLTLT và/hoặc H/C BQ tăng hoạt có ĐNVD

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