Desmopressin Oral Lyophilisate Lessens The Burden Of Nocturia In The Post-TURP Men Sooner They Go Asleep – An Action Unreachable By Fluid Restriction Alone But Attenuated By Aging

Abstract
626

Introduction & Aims of study: Desmopressin Oral Lyophilisate (“DRUG”) possesses reliable bioavailability and fast action in handling water in renal tubules in young people (1). Persistent nocturia in men following TURP for LUTS / AUR is common but short of effective treatment (2). This study explored the action & clinical efficacy of “DRUG” in treating post-TURP nocturia by:

(A) Comparing
(i) its dynamic action [ variation of the average hourly urine excretion rate (“UER”) across the bedtime period ] with placebo
(ii) the reduction of the hourly “UER” by “DRUG” ( “AUER”subgroup ) between young (≤ 70yo.o) and old (> 70yo.o) post-TURP men;
(iii) the time elapsed (a) between retiring to bed and 1st nocturia (“1stNtime”) before and after the treatment (“Tx”) & (b) between placebo and “DRUG”

(B) Determining the cut-off value of post intervention “1stNtime” with which to characterize subjective improvement of the nocturia and satisfaction with “Tx” by the men.

Study design: Prospective, Randomized, Double Blind, Placebo-controlled trial (RCT)
Materials and Methods: Subjects: Post-TURP men (N=47) with persistent nocturia (≥ 3 months & ≥ 2 per night by voiding diary) ; Nocturnal Polypuria: N=45; [ Age of subjects (y.o.): mean=69.5, range 57-75; uro. n=24; ≥70yo. n=23] Weight of subjects (kg): mean=86.7, range 47-86; Peak micturition flow (Gmax) [ml/sec] = mean=15.8, SD 7.9; Voided volume (ml): mean=294; Post-void residual (PVR)(ml): mean=60, SD 48.5.

Intervention: “DRUG” 60ug (N=22) vs Placebo (N=25)

Data collection: Voiding diary x 4 consecutive days before “Tx” & in the last 4 days of “Tx” and questionnaire for global impression of “Tx”.

Variables derived from voiding diary: Average hourly “UER” (ml/hour) = [volume of voided urine divided by time elapsed between 2 voidings ] spanning across the bedtime (pre-Tx & post-Tx)

hourly “AUER”, placebo = [UERpost-Tx – UERpre-Tx] / DRUG across bedtime
hourly “AUER”, placebo = [UERpost-Tx – UERpre-Tx] / Placebo across bedtime

Outcome: Comparison of “AUER” at >0.05 (p=0.018) in placebo & >0.05 (p=0.018) in “DRUG” & vs “AUER” at 0.05 (p=0.018) across bedtime between placebo & “DRUG”.

“1stNtime” placebo vs “1stNtime” placebo across bedtime

Subjective perception of the outcome (improvement of nocturia and satisfaction with “Tx”): “TIME”

Statistical tests: paired t test / f test (parametric data);
Wilcoxon rank sum test (non-parametric data) ; chi-square test (categorical data) ; ROC curve analysis for “TIME”; p value denoted < 0.05

Results: Nocturia was lessened in “DRUG” [ (↓ 37% ) as compared to placebo gp (↓ 15% ) ] in men ≤70y.o. but not in men >70y.o. ROC analysis showed that “TIME” = 185 min ( p=0.071, p=0.018 ) and 211 min ( AUC = 0.661, p=0.051 ) are to regard the “Tx" as being able to improve nocturia (185 min ) and "Tx" result as being satisfactory ( 211 min ) , respectively. Other results are tabulated in table 1.

Interpretation of result: Both groups of men had readily reduced their daily fluid intake after the recruitment by “11-12% associated with significant and similar reduction of nocturnal urine output and nocturnal episodes after “Tx” (Table 1). However, only men receiving “DRUG” could remarkably extend “1stNtime” (from 140 to 219 min; >0.05) associated with the drastic “TIME” = 229 min ( ↓ 45% )[ Fig 1 & 2 ] in the early hours of sleep. This observation failed to be replicated just by restricting fluid intake alone, whereby the much wanted “decreased nocturnal urinary production” merely appeared in the latter hours in bed (placebo group Fig 1) in which older adults (> 60y.o) are less able to get deep & restorative sleep (3). Patients with high percutaneous clinical benefits provided that “1stNtime” can be prolonged to at least 3 – 3.5 hours (“TIME”). Of note, this action profile (“AUER”subgroup) is less pronounced in men > 70 y.o., being of lower magnitude (40% less), shorter duration of action (~ 3 hrs shorter ) [ Fig 2 ] & uncertain reduction in nocturia.

Concluding message: Desmopressin Oral Lyophilisate lessens the burden of nocturia by remarkably prolonging the time to first nocturia in post-TURP men mainly via its action profile in the early phase of the sleep which this profile tends to diminish.

Table 1.

Comparison between Placebo gp and “DRUG” gp for parameters derived from voiding diary

Disclosures: Funding: Research Grant from Dept. of Surgery, The Chinese University of Hong Kong Clinical Trial: Yes; Registration Number: The Chinese University of Hong Kong CUHK_CCT00455 RCT: Yes Subjects: HUMAN ETHICS COMMITTEE: The Joint Chinese University of Hong Kong – New Territories East Cluster Clinical Research Ethics Committee (The Joint CUH-NTEC CREC) Helsinki: Yes Informed Consent: Yes

References
3. Wright K, Frey DJ Age-related changes in sleep and circadian physiology, from brain mechanisms to sleep behaviour. Geriatric Medicine, 2008, Informa Healthcare

Contact
Jeremy Y. C. TEOH
Division of Urology, Dept. of Surgery
The Chinese University of Hong Kong
E-mail: jeremytoeh@surgey.cuhk.edu.hk
Phone: (852) 3505 1663

Statistical analyses were performed using the Statistical Package for Social Sciences (SPSS) software, version 15.0.