PRIZE AWARD: Innovative Research Presented on Nocturnal Voiding Problems

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DEVELOPMENT OF A SHORT-FORM FOR EVALUATING THE PATHOPHYSIOLOGIC MECHANISMS OF NOCTURIA.

Hypothesis / aims of study

Nocturia is one of the most prevalent and bothersome lower urinary tract symptoms and is associated with nocturnal polyuria in 75% of the cases (1,2). This is attributed to disturbances in water diuresis, which is regulated by vasopressin, and solute diuresis, that is controlled by aldosterone and the atrial natriuretic peptide (ANP) (3). Since abnormalities can occur in each of these regulating mechanisms and manifest at different moments during the day, we perform 24h urinary osmolality tests in order to identify the pathophysiological mechanisms of nocturnal polyuria. Unfortunately, this is an extensive and burdensome test because a urine sample is collected every 3 hours during 24h, resulting in a total of 8 samples.

The objective of this study was to evaluate the differences in 24h urinary osmolality between an adult nocturia population and controls. Second, we figured out how we could simplify this test without compromising the obtained information. To enable comparisons between day and night excretions, we searched for 1 representative sample for the day and 1 representative sample for the night instead of 8 urine samples during 24h.

Study design, materials and methods

Since October 2011, 80 nocturic adults and 41 controls were included. As part of the study protocol, all participants were requested to collect a urine sample every 3 hours during 24h to determine levels of creatinin, urea, osmolality and sodium and subsequently, solute and sodium excretion was calculated. The last 3 samples (12-2am, 3-5am, 6-8am) were considered as nighttime samples in all subjects.

A paired Student's t-test was used to analyse variables within both groups and an independent Student's t-test to assess differences between the two groups. Linear regression was performed with the mean nocturnal (or daytime) excretion of one of the substances as dependent variable and the 3 (or 5) individual samples that represented the night (or day) as independent variables.

Results

Mean age of the total group was 55.89±17.2, 46,3% female and 53,7% male. A comparison between the nocturia group (n=80) and control group (n=41) for the mean values of sodium, solute, osmolality and urea excretion are represented in table 1.

Table 1: The 24h urinary osmolality profile in patients with nocturia and controls

	Nocturia (n=80)			**Controls (n=41)**			**P-value**	
	Day (mean±SD)	Night (mean±SD)	P-value	Day (mean±SD)	Night (mean±SD)	P-value	Day	Night
Sodium excretion [(mmol/l)/(mg/dl creatinin)]	1,3±0,5	1,5±0,6	0,007*	1,2±0,5	1,1±0,6	0,203	0,553	0,002*
Solute excretion [(mosm/kg)/(mg/dl creatinin)]	6,8±1,6	6,8±1,7	0,961	6,4±1,5	5,7±1,8	0,007*	0,157	0,001*
Osmolality [mosm/kg]	525,8±165,0	485,7±152,7	0,009*	617,0±221,9	590,5±240,5	0,427	0,012*	0,004*
Urea excretion [(g/l)/(mg/dl creatinin)]	0,17±0,04	0,18±0,05	0,009*	0,16±0,03	0,18±0,1	0,313	0,286	0,838

* P-value<0,01

Daytime samples were collected between 9-11am (U1), 12-2pm (U2), 3-5pm (U3), 6-8pm (U4) and 9-11pm (U5), while nighttime samples were collected between 12-2pm (U6), 3-5am (U7) and 6-8am (U8). The sample that correlated the best with the mean daytime excretion of the different variables was almost always the sample between 6 and 8pm (U4). The sample between 3 and 5am (U7) was the most representative for mean nighttime excretion.

Table 2: Optimal correlation of the individual nighttime (or daytime) sample with the mean values of nighttime (or daytime) excretion for the different variables

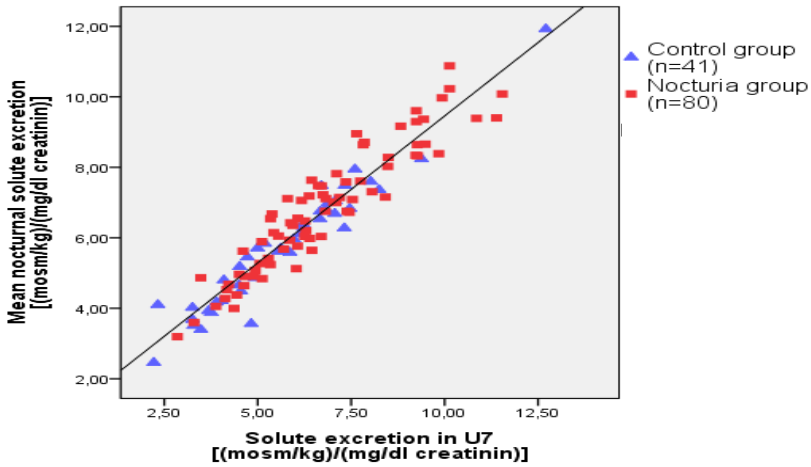
	Daytime excretion (U1-U5)				**Nighttime excretion (U6-8)**			
	Nocturia	R^2	Control	R^2	Nocturia	R^2	Control	R^2
Sodium excretion [(mmol/l)/(mg/dl creatinin)]	U4	0,744	U4	0,749	U7	0,848	U7	0,900
Solute excretion [(mosm/kg)/(mg/dl creatinin)]]	U2*	0,749	U4	0,778	U7	0,875	U7	0,930
Osmolality [mosm/kg]	U4	0,695	U4	0,783	U7	0,791	U7	0,901
Urea excretion	U4	0,781	U3**	0,810	U7	0,906	U7	0,990

[(g/l)/(mg/dl creatinin)]								

*U4: R^2 = 0,736; ** U4: R^2 = 0,768

The correlation of solute excretion in sample U7 (3-5am) and the mean nocturnal solute excretion are represented in figure 1 for both nocturic patients and controls.

Figure 1: Correlation of solute excretion in U7 (3-5am) and mean nocturnal solute excretion in the nocturia (R^2 = 0,875) and control group (R^2 = 0,930)



Interpretation of results

Comparing mean values during day and night within nocturic group and controls:

During the night, the nocturic patients showed a significant decrease in osmolality and increase in sodium excretion, which causes respectively water and solute diuresis. This circadian rhythm was not observed in the controls, in whom only solute excretion decreased significantly during the night.

Comparing nocturic group with controls:

At any time, nocturic patients had significantly less concentrated urine, which reflected the influence of vasopressin. Also the nocturnal loss of solutes, which is regulated by aldosterone and ANP, was significantly higher in the nocturic population and could be explained by a significant increase in nocturnal sodium loss, which was only observed in the nocturia group.

Simplification of 24h osmolality test:

Instead of collecting 8 urine samples to determine the underlying cause(s) of nocturnal polyuria, we documented that one sample during the day and one during the night is sufficient to assess the circadian rhythm of sodium, solutes, osmolality and urea excretion. One urine sample between 6 and 8pm was representative for the mean daytime excretion. There were two exceptions but the R^2-value was very close to that of the sample between 6 and 8pm. One urine sample between 3 and 5am was representative for the mean nighttime excretion.

Concluding message

Assessment of the pathophysiologic mechanisms of nocturnal polyuria, which is major cause of nocturia, can be simplified. The 8 urine samples requested to evaluate the circadian rhythm of sodium, solutes, osmolality and urea excretion can be replaced by one daytime sample between 6 and 8pm and one nighttime sample between 3 and 5am to evaluate differences between day and night excretion.

References

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