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GENDER DIFFERENCES IN DIURESIS, WITH A FOCUS ON COPEPTIN

Hypothesis / aims of study

Urine production is influenced by glomerular filtration rate, osmotic diuresis and water diuresis[1]. Vasopressin is the main hormone responsible for the regulation of free water excretion, while the atrial natriuretic peptide (ANP) and the renin-angiotensin-aldosterone system (RAAS) regulate solute and sodium clearance. Sex hormones influence all three of these hormones, for example vasopressin concentrations fluctuate during the menstrual cycle[2]. This might be an explanation for the gender differences in lower urinary tract symptoms. We aimed to investigate the influence of gender on the diurnal regulation of urine production with special focus on copeptin, which may be a surrogate for vasopressin.

Study design, materials and methods

In order to demonstrate the effect of gender on urine production we merged 2 databases from 2 different observational prospective studies. In both studies, patients were asked to complete a renal function profile. This means participants were required to collect a urine sample every three hours for a period of 24 hours. Collection started after the first morning void of day 1 and ended after the first morning void of day 2. The first five samples were considered daytime samples, the last three nighttime samples. Volume of each sample, and of each micturition in between had to be noted, to calculate the 24h urine volume. Sodium, osmolality and creatinine was measured on each of the samples. Concentrations of serum osmolality, sodium, creatinine were analyzed and used to calculate the renal clearance of each of these substances (Usubst x Uflow /Psubst). Copeptin was measured on plasma samples, that were stored at -80°C, until time of analysis. Medians and interquartile ranges are recorded as descriptive statistical parameters. Comparisons between groups were performed using the Mann-Whitney U rank test for two independent samples. A p - value <0.05 was considered statistically significant.

Results

In order to correct for changes during the menstrual cycle and menopause, we selected more females, and excluded all patients above 50 years old. We included 46 participants, of which 31 were female (67%). There was no difference in age between females (35 (IQR 23 – 43)) and males (29 (IQR 24 – 42)) (p=0.991). Although there was no difference in urinary osmolality (p=0.053), total voided volume (p=0.419) or diuresis rate between both groups (p=0.460), nighttime diuresis rate was higher in males compared to females (p=0.041). Men clearly had a higher sodium clearance than women (p=0.011), and a higher reabsorption of free water (p=0.008). Differences in the renal function profile parameters are shown in table 1 and figure 1. Copeptin was lower in females (3,02 (IQR 2,08 – 3,65) compared to males (4,64 (3,68 – 6,57) (p=0.002).

Interpretation of results

This study shows a significant difference in urine production between males and females. The higher sodium clearance and water reabsorption in males might be explained by the effect of androgens on ANP and vasopressin. By measurement of copeptin, we could demonstrate a difference in vasopressin between both genders. In contrast, urine volume and urinary osmolality did not differ between the groups, we can interpret this as a higher sensitivity of females to vasopressin. In this population, males had a higher nighttime diuresis rate, but this might be a coincidental finding.

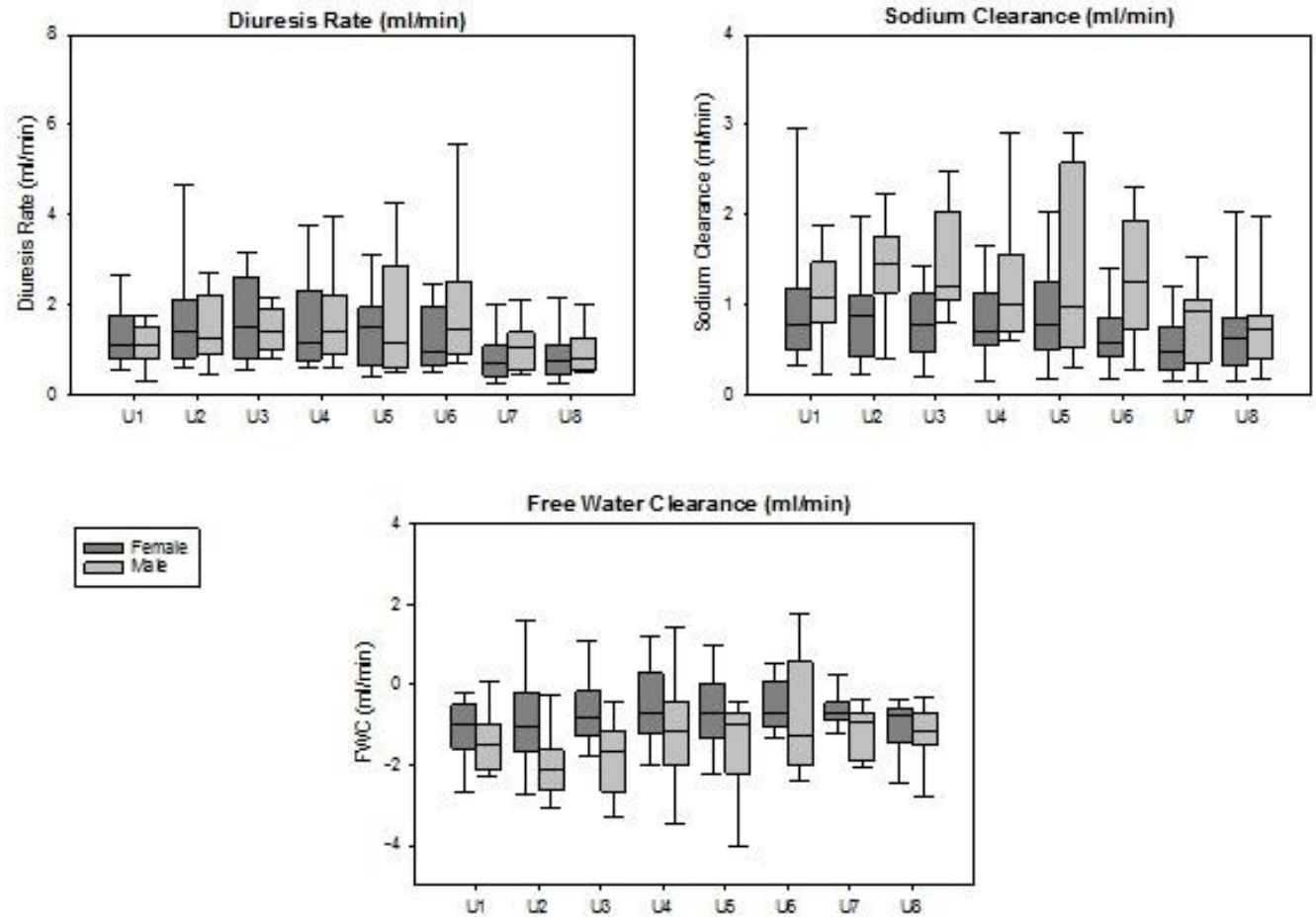
Concluding message

We demonstrated a difference in urine production, both osmotic and free water diuresis, between males and females. Copeptin in higher is males than females, which can be an argument for the higher sensitivity of females to vasopressin. Further research is needed to ascertain the effect of sex hormones on lower urinary tract symptoms.

Table 1: Characteristics of the renal function profile

	Female	Male	p-value
Total voided volume (ml)	1675 (1260 – 3170)	2150 (1555 – 2680)	0.419
Daytime voided volume (ml)	1310 (825 – 2025)	1300 (1125 – 1625)	0.833
Nighttime voided volume (ml)	450 (325 – 760)	560 (500 – 1060)	**0.041**
Diuresis rate daytime (ml/min)	1,46 (0,92 – 2,25)	1,43 (1,25 – 1,81)	0.824
Diuresis rate nighttime (ml/min)	0,83 (0,60 – 1,41)	1,04 (0,93 – 1,92)	**0.050**
Sodium clearance day (ml/min)	0,89 (0,56 – 1,16)	1,16 (1,01 – 1,63)	**0.007**
Sodium clearance night (ml/min)	0,58 (0,38 – 0,88)	0,92 (0,72 – 1,42)	**0.030**
Free water clearance day (ml/min)	-0,81 (-1,42 – 0,01)	-1,56 (-2,18 – -1,01)	**0.004**
Free water clearance night (ml/min)	-0,77 (-1,06 – -0,37)	-1,05 (-1,74 – -0,26)	0.155

Figure 1: Diuresis rate, sodium and free water clearance in females compared to males



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