

## DIURNAL VARIATION OF COPEPTIN, A SURROGATE OF VASOPRESSIN

### Hypothesis / aims of study

A low nocturnal vasopressin is thought to be one of the causes of increased nocturnal urine production, thus leading to nocturnal polyuria and nocturia. Secretion of vasopressin is triggered by small changes in plasma osmolality, but the half-life of the hormone is short, making it difficult to measure. Copeptin is co-secreted with vasopressin, and in contrast to vasopressin, it is a stable parameter and measurement is less expensive.<sup>1</sup> In a previous study we found that random copeptin samples cannot be used to identify patients with nocturnal polyuria. We set up this study to determine the best conditions (fasting, fluid restriction, ...) and the best timing (morning, daytime, ...) to take a blood sample for measurement of copeptin.

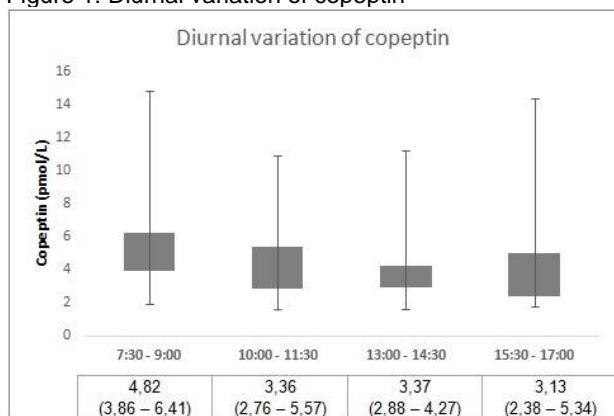
### Study design, materials and methods

In September 2015, 24 volunteers were included in this observational prospective study. A blood sample was taken at four different time points during the day for measurement of copeptin. The first (T1) was a sober morning sample, at this time we also measured serum sodium, creatinine and osmolality. The second sample (T2) was taken between 10:00 and 11:30, the third (T3) between 13:00 and 14:30 and the last (T4) between 15:30 and 17:00. At time of blood sampling, a urine sample was provided as well. Volume of each sample had to be noted, and osmolality, sodium and creatinine were measured on each of these urine samples, to calculate the renal clearance of these substances. Medians and interquartile ranges are recorded as descriptive statistical parameters. Mann-Whitney U and Kruskal-Wallis analysis of variance and Spearman's correlation analysis were used for statistical analysis. A p-value <0.05 was considered statistically significant.

### Results

Median age was 27 (25 - 32), 12 participants were female (50%). Only one of the volunteers had nocturnal polyuria (female, aged 53 year old, NP<sub>i</sub> = 34%). The copeptin concentration of the sober morning sample was higher than the other samples (p= 0.03, Fig 1). We confirmed lower copeptin samples in females (3,13 pmol/L (IQR 2,36 – 4,19)) compared to males (5,14 pmol/L (IQR 3,64 – 8,55)) (p<0.001). A positive correlation was found between copeptin and urinary osmolality of the corresponding urine sample (p<0.001), and mean daytime urinary osmolality (p=0.01). Copeptin was negatively correlated with diuresis rate (p<0.001) and free water clearance (p=0.001). No correlation was found with plasma osmolality.

Figure 1: Diurnal variation of copeptin



### Interpretation of results

We can conclude that diurnal variation in controls is limited with slightly higher values in the morning. This can be explained because vasopressin, and thus, copeptin, rises during the night, and can be expected to remain high in the morning before eating or drinking. We have to note that this is a very young population, not characteristic for the population that mostly presents with nocturnal polyuria. In this study we did not take a late evening blood sample, since we reasoned there is no immediate clinical use, as patients do not visit the clinic and have their blood taken late at night.

### Concluding message

This study suggests that sober morning copeptin samples may be an interesting path in the investigation of nocturia and nocturnal polyuria, but further research is necessary to confirm these results in a nocturia population.

### References

- Morgenthaler N., Struck J., et al. Assay for the measurement of copeptin, a stable peptide derived from the precursor of vasopressin. Clin Chem. 2006 Jan;52(1):112-9

### Disclosures

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