🏆 Award for Innovative Research Presented on Nocturnal Voiding Problems

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HAPTOGLOBIN POLYMORPHISM – AN EXPLANATION FOR GLOBAL POLYURIA?

Hypothesis / aims of study

Haptoglobin (Hp) is an acute-phase, haemoglobin-binding plasma protein that occurs in three different phenotypes: Hp1-1, Hp2-1 and Hp2-2. This polymorphism is associated with functional differences, leading to important clinical consequences. For example, Hp1-1 phenotypes show higher blood pressures and are more likely to be salt-sensitive, while Hp2-2 phenotypes are more likely to be salt-resistant (1-2). Because (nocturnal) polyuria has also been related to alterations in blood pressure and disorders in sodium clearance, the aim of this study was to explore associations between Hp-polymorphism and diuresis rate in adults.

Study design, materials and methods

This prospective, observational study consisted of a haptoglobin phenotyping (starch-gel electrophoresis of haemoglobin-supplemented serum) in adults who completed a renal function profile between October 2011 and February 2015. This is a 24h urine collection in which 8 urine samples with an interval of 3 hours between each sample was collected (10h-13h-16h-19h-22h-01h-04h-07h) to determine voided volume and urinary levels of osmolality and sodium. Serum osmolality and sodium were analysed to calculate renal clearance. Global polyuria was defined as a urine production >40ml/kg bodyweight/24h. The median and interquartile range were recorded as descriptive statistical parameters. Differences between groups were assessed using the chi-square test for dichotomous variables and the Mann-Whitney U test for nonparametric variables. Multiple logistic regression and odds ratios (ORs) were used to evaluate risk factors associated with global polyuria. A p-value <0.05 was considered statistically significant.

Results

A total of 177 subjects were eligible for analysis; 28 (16%) with Hp1-1, 91 (51%) with Hp1-2 and 58 (33%) with Hp2-2. Mean age was 65 (51-72) years and 63% of the participants were female (Table I). The three subgroups did not differ in terms of age, gender, BMI, 24h-urinary sodium excretion, 24h-urine production and presence of global polyuria. Comparing participants with Hp1-1 to those with Hp2-1 and Hp2-2 showed a significantly higher prevalence of global polyuria in the Hp1-1 group (p=0.045).

Table I: Characteristics of participants

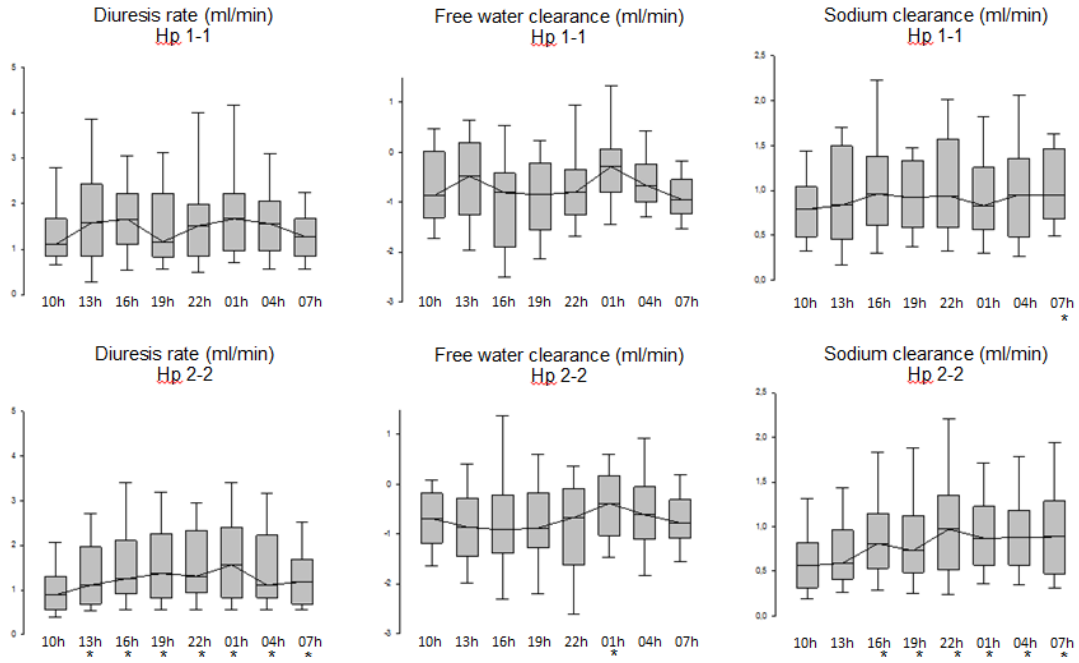
	Overall (n=177)	**Hp 1-1 (n=28)**	**Hp 2-1 (n=91)**	**Hp 2-2 (n=58)**	**Hp 2-1 + 2-2 (n=149)**	**P-value***
Age (yrs)	65 (51-72)	66 (55-71)	64 (48-69)	66 (53-74)	65 (50-72)	0.652
Gender (n(%) female)	111 (63)	15 (54)	59 (65)	37 (64)	96 (64)	0.277
BMI (kg/m²)	25 (23-28)	26 (24-30)	25 (22-27)	25 (23-28)	25 (23-28)	0.166
24h-urinary sodium excretion (mmol)	176 (135-176)	189 (141-248)	184 (136-224)	171 (119-222)	175 (133-223)	0.191
24h-urine production (ml/kg bodyweight)	28 (23-28)	29 (24-43)	28 (23-36)	30 (23-37)	28 (23-36)	0.322
Global polyuria (n(%))	32 (18)	9 (32)	14 (15)	9 (16)	23 (15)	**0.045**

**For comparison between Hp1-1 and Hp2-1+2-2*

The presence of Hp1-1 was significantly associated with global polyuria (OR 2.5 (1.0-6.2); p=0.044). Multiple logistic regression analysis adjusted by age, BMI and Hp2-2 phenotype showed a significant association between the presence of global polyuria and the Hp1-1 phenotype (β = -0.190; OR 0.304; 95%CI 0.106-0.871; p = 0.027) and male gender (β = 1.223; OR 3.398 95%CI 1.269-9.103; p = 0.01).

Diuresis rates of individuals with Hp1-1 and Hp2-2 are described in figure 1, and can be explained by variations in free water clearance and sodium clearance.

Figure 1: Diuresis rate, free water clearance and sodium clearance in individuals with Hp1-1 and Hp2-2



**p<0.05 for comparison with the value of the urine sample at 10h*

Interpretation of results

Participants with Hp1-1 have a greater risk for the presence of global polyuria. The diurnal variations in diuresis rate can be explained by variations in free water clearance, which occur at the same moments (13h and 01h). We hypothesise that the higher diurnal diuresis level can be explained by a diminished sodium clearance, which suits the finding that Hp1-1 is related to salt-sensitivity and hypertension because of the possible increase in intravascular volume by accumulation of sodium and water.
Participants with Hp2-2 are known to be salt-resistant, which is confirmed by the variations in sodium clearance, which was absent in the participants with Hp1-1.

Concluding message

Participants with Hp1-1 have a greater risk for the presence of global polyuria. Since Hp1-1 is associated with salt-sensitivity, future research has to evaluate the association between disturbed sodium clearance and global polyuria, and the role of sodium restriction as treatment of global polyuria in these patients.

References

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2. Averina VA, Othmer HG, Fink GD, Osborn JW. A mathematical model of salt-sensitive hypertension: the neurogenic hypothesis. The Journal of physiology. 2014.

Disclosures

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