

Are physiological stimuli for vasopressin release, assessed as copeptin concentration, operative in hemodialysis patients?

Esmée M. Ettema¹, Johanna Kuipers², Solmaz Assa¹, Henk Groen¹, Ron T. Gansevoort¹, Katrin Stade³, Stephan J.L. Bakker¹, Carlo A.J.M. Gaillard¹, Ralf Westerhuis² and Casper F.M. Franssen¹.

1. University Medical Center Groningen, University of Groningen, Groningen, The Netherlands. 2. Dialysis Center Groningen, Groningen, The Netherlands 3. Thermo Fisher Scientific BRAHMS GmbH, Hennigsdorf, Germany

Introduction

Plasma levels of the vasoconstrictor arginine vasopressin (AVP) are higher in hemodialysis (HD) patients compared with healthy individuals. However, AVP levels show little or no increase during HD and it has been suggested that inadequate release of AVP could play a role in the onset of intradialytic hypotension. Likewise, plasma levels of copeptin, a surrogate marker of the AVP, are increased in HD patients. Presently, it is unknown what drives copeptin levels in HD patients.

Aim

We investigated whether the established physiological stimuli for copeptin release, i.e. plasma osmolality, blood volume and blood pressure, are operative in HD patients.

Methods

108 prevalent HD-patients on a thrice-weekly HD schedule were studied during the first dialysis session of the week. Plasma levels of copeptin, sodium as the major determinant of plasma osmolality, NT-proBNP, blood volume and blood pressure were measured before and at the end of HD. Multivariate analysis was used to determine the association between copeptin and its stimuli pre-HD and during HD and these analyses were corrected for age, sex and diabetes.

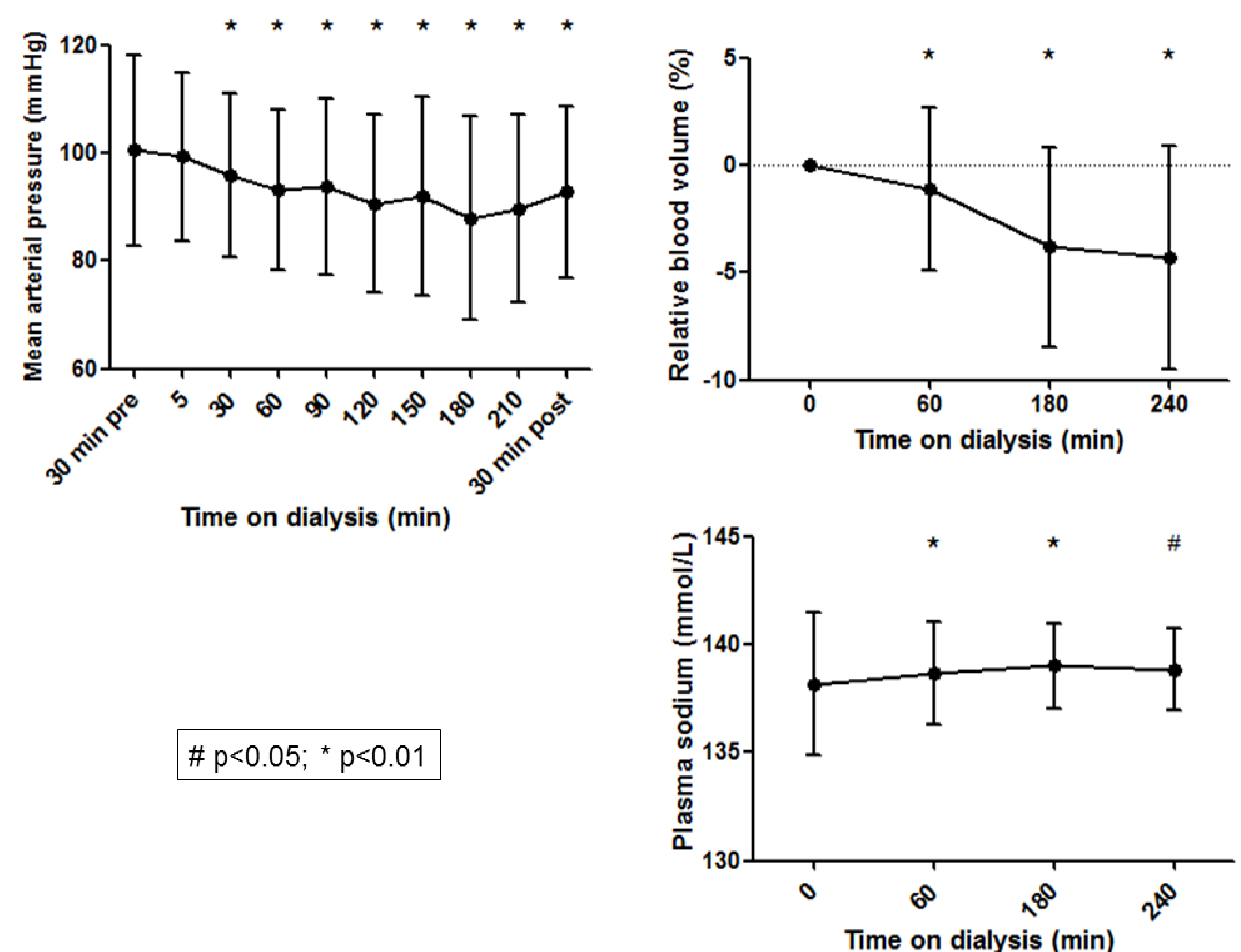
Results

Patient characteristics are shown in Table 1. Median pre-HD copeptin levels were 141.5 pmol/L (IQR 91.0–244.8 pmol/L). Pre-HD plasma sodium levels, plasma NTproBNP levels and mean arterial pressure were not significantly associated with higher plasma copeptin levels pre-HD. During HD, copeptin levels rose significantly from 141.5 to 164.0 pmol/L (IQR 98.3–292.0 pmol/L) at the end of dialysis ($p < 0.01$). Mean arterial pressure and blood volume decreased significantly during HD, whereas plasma sodium rose slightly but significantly (Figure).

Table 1. Patient characteristics

Age, years	63 ± 15.6
Males	65%
Dialysis vintage, months	20 (8-48)
Diabetes	23.1%
Residual diuresis ≥200 ml/day	36.1%
Hypertension	82.4%
Excess weight pre-HD, kg	2.2 (1.3 – 3.3)
Ultrafiltration volume, mL	2553 ± 777
Mean arterial pressure pre-HD, mmHg	100 ± 18
Sodium pre-HD, mmol/L	138 ± 3
NT-proBNP pre-HD, pg/mL	3966 (1737 – 8272)

Figure. Course of mean arterial pressure, blood volume and plasma sodium levels during HD



Greater decreases in blood volume and mean arterial pressure were associated with a greater increase in copeptin levels, whereas there was no significant association between the change in plasma sodium levels and the change in copeptin concentration during HD (Table 2).

Table 2. Association between the intradialytic change in sodium, mean arterial pressure and blood volume and the change in copeptin

Determinant	Multivariate linear regression			
	Adjustment for age, sex, diabetes		Fully adjusted model*	
	Beta _{standardized}	P-value	Beta _{standardized}	P-value
Δ sodium (mmol/L)	-0.010	0.660	-0.001	0.967
Δ MAP (mmHg)	-0.083	0.017	-0.051	0.044
Δ RBV (%)	-0.050	0.007	-0.057	0.007

* Adjustment for age, sex, diabetes and the determinants included in the model

Conclusion

1. Plasma copeptin levels are elevated predialysis and increase further during HD.
2. Volume stimuli, i.e. decreases in blood pressure and blood volume, rather than the change in plasma sodium are significantly associated with changes in plasma copeptin levels during HD.



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