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**Association between copeptin levels and treatment responses to hypertonic saline infusion in patients with symptomatic hyponatremia: A prospective cohort study**

**Seon Ha Baek**

*Hallym University Dongtan Sacred Heart Hospital, Korea*

**Background**

Copeptin is secreted in equimolar amounts as arginine vasopressin (AVP), the main hormone regulating body fluid homeostasis. A recent study reported a copeptin-based classification of osmoregulatory defects in syndromes of inappropriate antidiuresis that may aid in prediction of therapeutic success. We investigated the usefulness of copeptin for differentiating etiologies of hyponatremia and predicting the efficacy and safety of hypertonic saline treatment in hyponatremic patients.

**Methods**

We performed a multicenter, prospective cohort study of 100 inpatients with symptomatic hyponatremia (corrected serum sodium [sNa]  $\leq 125$  mmol/L) treated with hypertonic saline. Copeptin levels were measured at baseline and 24 hours after treatment initiation, and patients were classified as being below or above the median of copeptin at baseline or at 24 hours, respectively. Correlations between target, under correction, and overcorrection rates of sNa within 24 hours/24-48 hours and copeptin levels at baseline/24 hours were analyzed.

**Results**

Mean sNa and median copeptin levels were 117.9 mmol/L and 16.9 pmol/L, respectively. The ratio of copeptin to urine sodium allowed for an improved differentiation among some (insufficient effective circulatory volume), but not all hyponatremia etiologic subgroups. Patients with below-median copeptin levels at baseline achieved a higher target correction rate in 6/24 hours (odds ratio [OR] 2.974,  $P=0.024$ ; OR 6.212,  $P=0.006$ ). Patients with below-median copeptin levels 24 hours after treatment showed a higher overcorrection rate in the next 24 hours (OR 17.997,  $P=0.020$ ).

**Conclusions**

There is a limited diagnostic utility of copeptin for differential diagnosis of hyponatremia. However, copeptin might be useful for predicting responses to hypertonic saline treatment in hyponatremic patients.

Box plot for copeptin levels (A) and copeptin-to-urine Na x 100 (B) according to etiologies of hyponatremia

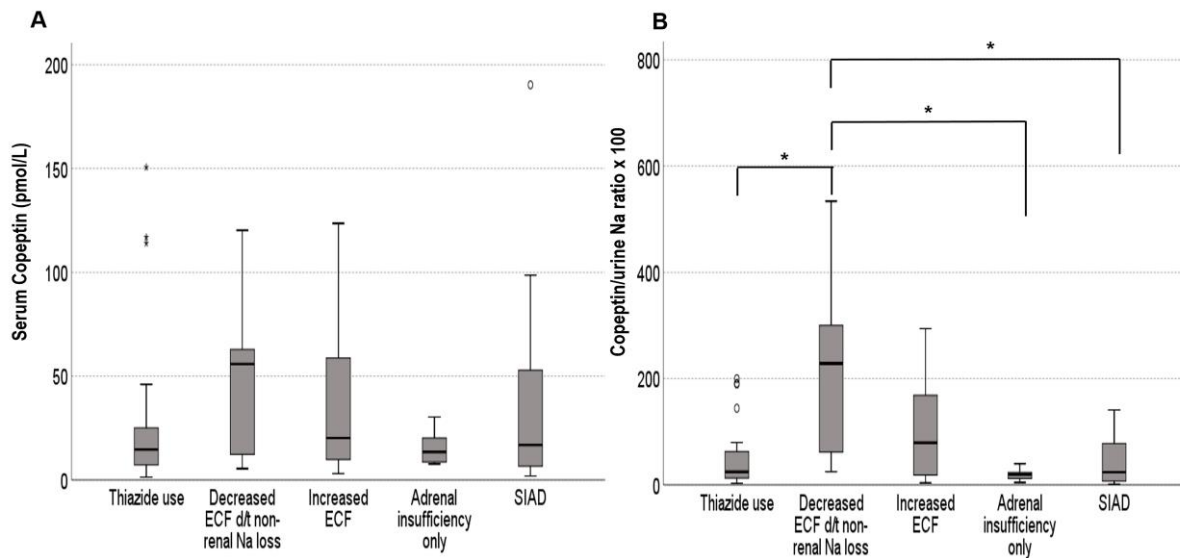


Table 1 Adjusted odds ratios for association between copeptin below the median at baseline and outcomes

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	Number	Univariable		Multivariable <sup>a</sup>		Multivariable <sup>b</sup>	
		OR (95% CI)	P-value	OR (95% CI)	P-value	OR (95% CI)	P-value
<b>Copeptin at baseline (low, high)</b>							
Under correction within 6hrs	(17/49, 21/49)	0.708 (0.313-1.602)	0.408	0.704 (0.310-1.596)	0.400	0.320 (0.101-1.020)	0.054
Target correction within 6hrs	(30/49, 17/49)	2.972 (1.306-6.764)	<b>0.009</b>	3.118 (1.346-7.223)	<b>0.008</b>	2.974 (1.157-7.643)	<b>0.024</b>
Overcorrection within 6hrs	(1/49, 4/49)	0.234 (0.025-2.177)	0.202	2.227 (0.023-2.239)	0.204	0.000 (0.000)	1.000
Under correction within 24 hrs	(2/49, 6/49)	0.305 (0.058-1.593)	0.159	0.306 (0.057-1.637)	0.166	0.000 (0.000)	0.993
Target correction within 24 hrs	(26/49, 18/49)	1.947 (0.868-4.366)	0.106	2.007 (0.882-4.568)	0.097	6.212 (1.671-23.089)	<b>0.006</b>
Overcorrection within 24 hrs	(11/49, 11/49)	1.000 (0.387-2.583)	1.000	0.916 (0.335-2.507)	0.865	0.435 (0.068-2.771)	0.379
<b>Copeptin at 24 after treatment (low, high)</b>							
Under correction within 24-48 hrs	(9/47, 19/50)	0.386 (0.153-0.974)	<b>0.044</b>	0.377 (0.147-0.969)	<b>0.043</b>	0.276 (0.031-2.490)	0.251
Target correction within 24-48 hrs	(27/47, 27/50)	1.150 (0.516-2.565)	0.733	1.157 (0.517-2.590)	0.723	0.768 (0.253-2.331)	0.641
Overcorrection within 24-48 hrs	(10/47, 2/50)	6.486 (1.339-31.415)	<b>0.020</b>	6.486 (1.339-31.415)	<b>0.020</b>	17.997 (1.592-203.452)	<b>0.020</b>

Abbreviations: OR, odds ratio; hrs, hours

Multivariable<sup>a</sup> age, sex; multivariable<sup>b</sup> age, sex, body mass index, systolic blood pressure, diabetes mellitus, liver cirrhosis, cancer, serum sodium/creatinine/uric acid/c-reactive protein/serum osmolality/urine osmolality/urine sodium at baseline, cause of hyponatremia, hypertonic saline volume, infusion mode of hypertonic saline (bolus/continuous/mixed)