Copeptin as a marker for severity and prognosis of aneurysmal subarachnoid hemorrhage



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Introduction

Grading of patients with aneurysmal subarachnoid hemorrhage (aSAH) is often confounded by seizure, hydrocephalus or sedation and the prediction of prognosis remains difficult. Recently, copeptin has been identified as a serum marker for outcomes in acute ischemic stroke and intracerebral hemorrhage (ICH). We investigated whether copeptin might serve as a marker for severity and prognosis in aSAH.

Methods

Eighteen consecutive patients with SAH had plasma copeptin levels measured with a validated chemiluminescence sandwich immunoassay. The primary endpoint was the association of admission copeptin levels with the World Federation of Neurological Surgeons (WFNS) grade score after resuscitation. Levels of copeptin were compared across clinical and radiological scores as well as between patients with ICH, intraventricular hemorrhage, hydrocephalus, vasospasm and ischemia



Results

The study included 18 patients (12 women and 6 men), median age of 57 years (interquartile range (IQR) [48-67]). Overall median copeptin level at admission was 17.0 pmol/L (IQR 3.3-38.4). Copeptin levels had a significant association with the severity of SAH measured by WFNS grade (P=0.006), the amount of subarachnoid blood (P=0.03) and the occurrence of ICH (P=0.02). There was also a trend between copeptin levels and functional clinical outcome at 6-months (P=0.054). No other clinical outcomes showed any statistically significant association. Admission copeptin levels might not predict later cerebrovascular events, yet serial testing throughout might show an association.

	n	Median copeptin level (IOR)	p-value
		(pmol/L)	
WFNS grade [*]			
Good-grade	11	6.8 (6.6-17.4)	
Poor-grade	7	26.3 (18.3-204)	P=0.006
Fisher grade			
Diffuse blood			
(Fisher grade 2 and 4)	3	1.6 (1.5-3.3)	
Thick clot	15	18 3 (6 8-60 4)	P=0.027
(Fisher grade 3)	15	10.5 (0.0 00.4)	F-0.027
ICH			
Yes	6	52.5 (17.4-204)	
No	12	6.7 (2.2-22.3)	P=0.02
IVH			
Yes	11	17.4 (6.6-38.4)	
No	7	7.1 (1.6-79.9)	P=0.89
Hydrocephalus			
Yes	12	17.9 (5-32.4)	
No	6	6.7 (3.3-60.4)	P=0.682
Vasospasm			
Yes	5	26.3 (24.5-60.4)	
No	13	7.1 (2.8-18.3)	P=0.15
Ischemia			
Yes	3	24.5 (1.3-60.4)	
No	15	16.5 (3.3-38.4)	P=1.0
Outcome ^b	1.0000		
Good	13	6.8 (2.8-24.5)	
Poor	5	26.3 (17.4-204)	P=0.054
Mortality	× 5000	AND	
Survivors	14	7.0 (2.8-38.4)	
Deceased	4	21.9 (17-115.2)	P=0.277

Conclusions

Copeptin may indicate clinical severity of the initial bleeding and may therefore help in guiding treatment decisions in the setting of aSAH. These initial results show that copeptin might also have prognostic value for clinical outcome in SAH.

Learning Objectives

By the end of this session the audience should know 1)about the possible usefulness of Copeptin as serum marker in SAH

2)that Copeptin is associated with the severity of SAH, the amount of subarachnoid blood and the occurence of ICH

References

1. Report of World Federation of Neurological Surgeons Committee on a Universal Subarachnoid Hemorrhage Grading Scale J Neurosurg 1988;68:985-986.

2. Bederson JB, Connolly ES, Jr., Batjer HH et al. Guidelines for the management of aneurysmal subarachnoid hemorrhage: a statement for healthcare professionals from a Special Writing Group of the Stroke Council, American Heart Association Stroke 2009;40:994-1025.

3. Le Roux PD, Elliott JP, Newell DW et al. Predicting outcome in poor-grade patients with subarachnoid hemorrhage: a retrospective review of 159 aggressively managed cases J Neurosurg 1996;85:39-49.

4. Morgenthaler NG, Muller B, Struck J et al. Copeptin, a stable peptide of the arginine vasopressin precursor, is elevated in hemorrhagic and septic shock Shock 2007;28:219-226.

5. Zweifel C, Katan M, Schuetz P et al. Copeptin is associated with mortality and outcome in patients with acute intracerebral hemorrhage BMC Neurol 2010;10:34.

6. Katan M, Fluri F, Morgenthaler NG et al. Copeptin: a novel, independent prognostic marker in patients with ischemic stroke Ann Neurol 2009;66:799 -808.

7. Macdonald RL, Higashida RT, Keller E et al. Preventing vasospasm improves outcome after aneurysmal subarachnoid hemorrhage: rationale and design of CONSCIOUS-2 and CONSCIOUS-3 trials Neurocrit Care 2010;13:416-424.

8. Fisher CM, Kistler JP, Davis JM. Relation of cerebral vasospasm to subarachnoid hemorrhage visualized by computerized tomographic scanning Neurosurgery 1980;6:1-9.

9. Kothari RU, Brott T, Broderick JP et al. The ABCs of measuring intracerebral hemorrhage volumes Stroke 1996;27:1304-1305.

10. Lackner P, Dietmann A, Beer R et al. Cellular microparticles as a marker for cerebral vasospasm in spontaneous subarachnoid hemorrhage Stroke 2010;41:2353-2357.

11. Zhu XD, Chen JS, Zhou F et al. Detection of copeptin in peripheral blood of patients with aneurysmal subarachnoid hemorrhage Crit Care 2011;15:R288.