Prognostic Factors of Neuroinflammation and Oxidative Stress in Brain Injury Patients at Dr. Cipto Mangunkusumo Hospital Jakarta

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Introduction

This study aims to determine the association between neuroinflammation and oxidative stress with prognosis of brain injury patients and the association between neurosurgical procedure with the neuroinflammation and oxidative stress condition.

Methods

The study design is a prospective observation of 40 brain injury patients who underwent surgery. IL-6, uric acid, MDA, NR2A antibodies and GSH serum level of pre- and 1 day post-operation on brain injury patients were measured, and their association with GCS, GOS and neurosurgical procedures were analyzed.

Results

The post-operative IL-6 serum level showed a downward trend compared to pre-operative value (mean decrease: -190.61 pg/ml). The post-operative IL-6 level was significantly associated with GCS 7 days post-operation (p=0.006), with OR 24. The post-operative IL-6 serum level was significantly associated with GOS 3 months post-trauma (p=0.016) with OR 11.6. The post-operative uric acid serum level showed a downward trend compared to pre-operative value (mean decrease: -0.26 mg/dl). There was a significant difference between the mean of post-operative uric acid serum level in patients with 7 days post-trauma with GCS <8 (mean: 4.16 mg/dl) and GCS >8 (mean: 2.71 mg/dl), (p=0.042). The post-operative MDA serum level showed a downward trend compared to pre-operative value (mean decrease: -0,08 nmol/ml). There is no significant association between MDA serum level, GCS and GOS and no significant association between NR2A antibody and GSH serum level with GCS, GOS and neurosurgical procedure. From the multivariate analysis, the most important neuroinflammatory variable associated with GCS and GOS is IL-6.

Learning Objectives

Determine the association between neuroinflammation and oxidative stress with prognosis of brain injury patients and the association between neurosurgical procedure with the neuroinflammation and oxidative stress condition.

Conclusions

Neuroinflammation and oxidative stress may have prognostic values in brain-injured patients, in particular IL-6. Neurosurgical procedures may decrease the neuroinflammation process.

References

1.Paolin A, Nardin L, Gaetani P et al: Oxidative damage after severe head injury and its relationship to neurological outcome, Neurosurgery 51: 949-955, 2002

2.Chopp M, Mahmood A: Emerging treatments for traumatic brain injury, Expert Opinion on Emerging Drugs, 14(1):67-84, 2000

3.Woicienchowxky C, Schoning B, Cobanov J: Early IL-6 plasma concentration correlate with severity of brain injury and pneumonia in brain-injured patients: The Journal of Trauma, Infection and Critical vol.52, 329-45, 2002

4.Swartz KR, Liu F, Sewell D, Schocet T, Campbell I: Interleukin-6 promotes post-traumatic healing in the central nervous system, Brain Research, vol.896, 86-95, 2001

5.Schmidt OI, Infanger M, Heyde CE, Ertel W, Stahel F: The Role of Neuroinflammation in Traumatic Brain Injury, European Journal of Trauma, vol.30, 135-49, 2004

6.Dringen R, Gutterer JM, Hirrlinger J: Glutathione metabolism in brain, metabolic interaction between astrocytes and neurons in the defense against reactive oxygen species, European Journal of Biochemistry, Feb;267, 4912-16, 2000

7.Dambinova SA, Khounteev GA, Izykenova GA, Zavolokov IG, Ilyukhina AY, Skoromets AA: Blood test detecting autoantibodies to N-methyl-D-aspartate neuroreceptors for evaluation of patients with transient ischemic attack and stroke. Clin Chem. 49(10):1752-62, 2003

8.Bayir H, Kagan VE: Bench-to-bedside review: mitochondrial injury, oxidative stress and apoptosis – there is nothing more practical than a good theory. Crit Care. 12:206, 2008

9.Kinuta Y, Kimura M, Itokawa Y, Ishikawa M, Kikuchi H. Changes in xanthine oxidase in ischemic rat brain. J Neurosurg. 71:417-20, 1989

10.Pacher P, Nivorozhkin A, Szabo C. Therapeutic effects of xanthine oxidase inhibitors: renaissance half a century after the discovery of allopurinol. Pharmacol Rev. 58(1): 87-114, 2006

11.Higgins P, Walters M, Dawson J: The potential for xanthine oxidase inhibition in the prevention and treatment of cardiovascular and cerebrovascular disease. Cardiovascular Psychiatry and Neurology, Article ID 282059, 2009