

THE EFFECTS OF EXCITOTOXICITY WITH HYPOXIC-ISCHEMIC ENCEPHALOPATHY PIGLET MODEL

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Background: Glutamate was a major excitatory neurotransmitter in central nervous system (CNS). Neuronal death was caused by increase of glutamate. In neonatal hypoxic-ischemic encephalopathy (HIE), it was considered that this excitotoxicity enlarged the brain damage. In this study, we investigated the effect of glutamate in HIE model by using an antagonist of glutamate receptor, MK-801.

Methods: Piglets of 1-3 days old were anesthetized and ventilated. Animals were given 6% oxygen/ 94% nitrogen mixed gas for 45 minutes. Then they were resuscitated (HI group). In Hypothermia group, their oral temperature was cooled down by 3°C after the loading. In MK group, they were administrated MK-801 (10mg/kg i.p.) before the loading. Blood samples were obtained before and at 0, 4, 12 hours. Brain was obtained at 12 hours and iNOS protein was detected immunohistochemically.

Results: Plasma biopterin concentration was increased at 0 hour in HI and Hypothermia group. No significant change in biopterin was observed in MK group. In HI and MK group, iNOS-positive neurons were detected. In Hypothermia group, no iNOS-positive neurons were observed.

Discussion: As MK-801 blocked neuronal excitatory signal, it was considered that the iNOS was synthesized by another pathway. It was reported that HIF-1 was activated by hypoxia and it increased iNOS production. The rate-limiting enzyme of biopterin synthesis was GTP cyclohydrolase I, and it was activated by inflammatory cytokines. Our results suggested that the plasma biopterin level reflected the intensity of neuronal excitement.

Conclusion: Plasma biopterin concentration was useful to predict the severity of neonatal HIE.