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The effect of vitamin K2 (Menaquinone-4) on the cognitive impairments and anxiety in transient cerebral global Ischemia

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Background and Aim : Cerebral Ischemia is the second cause of fatality and the first cause of long-term disability in Iran. Based on statistics, every 5 minutes one person will face cerebral ischemia. In practice, stroke refers to a series of conditions caused by the occlusion or haemorrhage of blood vessels supplying the brain, which involves death and dysfunction of brain cells and neurological deficits. Vitamin K is a family of fat-soluble vitamins composed of naphthoquinone ring and a variable aliphatic chain that distinguishes two naturally occurring forms: vitamin K1 (Phylloquinone) and vitaminK2 (Menaquinone). Vit K2 is believed to prevent oxidative stress which is one of the causes of cell death in multiple disorders of the brain including Ischemia. This research is to investigate the effect of intraperitoneal injection of vitamin K2 on object recognition memory and anxiety in ischemic rats.

Methods : The adult Wistar male rats (200-250 gr) were randomly divided into four groups (n=5): Control, Ischemia, Ischemia+solvent (0.1% DMSO) and Ischemia+K2 (1mg/kg).the animals initially were subjected to surgery; the carotid vessels were blocked for 20 minutes. After 20 minutes of occlusion, vitamin K2 was injected during reperfusion followed by a second injection 1 hour later. After seven days of recovery, behavioral tests (NORT; Novel Object Recognition Task, EPM; Elevated plus maze) were taken.

Results : Vitamin K2 could significantly improve the function of object recognition memory tested with NORT in ischemic rats ($p<0.0001$). Vit K2 also significantly decreased the anxiety caused by ischemia induction ($p<0.01$) tested with EPM.

Conclusion : After stroke, the loss of ATP results ionic imbalance and this will cause calcium influx, at the same time release of glutamate will intensify calcium entry which can induce excitotoxicity. Loss of energy sources will also lead to mitochondrial dysfunction and generation of reactive oxygen species (ROS) and reactive nitrogen species (RNS). Excitotoxicity, ionic imbalance and oxidative/ nitrosative stress are believed to be the causes of cell

death.Vitamin K2 is an antioxidant and its activity might affect the redox-homeostasis of cells and tissues and can be considered as a regulatory factor in redox-signaling. Therefore,vitamin K2 probably prevents the oxidative stress in ischemic rats and has positive effects on recognition memory and decreasing anxiety. These assumptions are need to be further investigated.

Keywords : cerebral Ischemia; menaquinone-4; oxidative stress; anxiety; learning and memory