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The Alteration of Cognitive Function in Iron Overload Mice

Abstract—Regular blood transfusions is a lifetime treatment for blood disorder such as thalassemia and it can lead to the iron accumulation within the organs. Iron accumulation in the brain can cause toxicity by increasing reactive oxygen species (ROS) and altering apoptotic signal. However, the impact of the iron overload in cognitive function is still unclear. The purpose of this study is to investigate the effects of iron overload to the cognitive function of mice. Three groups of mice were divided into three groups with different dosing of iron injections (0, 0.1, and 0.3 mg/mice). Iron was injected intraperitoneally for 19 days. A special experimental maze was used to assess the cognitive function. The test was repeated three times; before injection, the 6th day of injection, and the 11th day of injection. After 19 days of injections, brain weight was measured and brain histology examined. Our results showed that cognitive function was impaired after iron injections. Cognitive function test indicated that the time required by group 1 during the first test were 265.20 ± 47.11 seconds, during the second test were 123.20 ± 18.33 seconds, and during the third test were 151 ± 45.80 seconds. Next, the time required by group 2 during the first test were 254.60 ± 44.16 seconds, during the second test were 176.60 ± 32.54 seconds, and during the third test were 259.60 ± 63.28 seconds. Then, the time required by group 3 during the first test were 260.20 ± 44.90 seconds, during the second test were 241.20 ± 32.65 seconds, and 272.40 ± 65.79 seconds during the third test. The data analysis indicated insignificant changes between group 1, group 2, and group 3 with p-value 0.068. There were no significant changes in brain weight and brain histology among all groups. We conclude that iron overload can cause alteration of mice cognitive function without change in brain histology

Keywords—Cognitive function, iron overload, special experimental maze

1 INTRODUCTION

According to Nagelhout [1], Thalassemia is a genetic disease caused by inherited mutations. It decreases either α -globin or β -globin synthesis chains in composing adult hemoglobin leading to anaemia, tissue hypoxia, and red cell hemolysis. It also relates to the imbalance in globin chain synthesis. Sir et al. [2] reported that the prevalence of thalassemia carriers in Southeast Asia is about 25-30%. Routine blood transfusion is a long-time treatment for these conditions. However, Hussain et al. [3] demonstrated that long-term blood transfusions would increase the serum iron level. According to Merono et al. [4], iron overload is defined as increase in iron deposition with or without tissue destructions. According to Whitney and Rolves [5], free iron is able to act as a free radical, could attack cell membrane, protein, and DNA.

White et al. [6] demonstrated that the iron excess could induce toxicity of brain cells by increasing Reactive Oxygen Species (ROS)

which is one of the oxidative stress sources and could initiate the apoptotic signal. Intracellular iron accumulation could be harmful towards some proteins, such as Ca^{2+} ATPase, a glutamate transporter, $\text{Na}^{+}\text{K}^{+}$ ATPase, ceramide, NMDA receptor, and sphingomyelin. Synapse dysfunction and necrosis of neuron could be caused by abnormalities in these proteins.

According to Blasco et al. [7], iron accumulation in some parts of the brain, such as the caudate nucleus, hypothalamus, and lenticular nucleus could decrease the cognitive function of the brain. Tucker et al. [8] demonstrated that iron excess could cause changes in the left hemisphere electroencephalography which is related to the cognitive function of the brain.

The mechanism underlying alteration of cognitive function due to iron excess remains uncertainty. The aim of this study is to investigate the effect of iron excess on the cognitive function of mice.