The Effect of Excess Iron on the Impairment of Glucose Metabolism in Mice

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Abstract— Excess iron in the body can trigger pathological conditions through production of reactive oxygen species (ROS) and the deposition in various organs. This condition can also disrupt whole metabolism process, including glucose metabolism. However, the mechanisms between iron and glucose metabolism remain unclear. The study was to investigate the effect of excess iron with glucose metabolism disorder by assessing Glucose Tolerance Test (GTT) and gluconeogenesis rate in mice through Intraperitoneal Glucose Tolerance Test (IPGTT) to determine insulin resistance, Intraperitoneal Pyruvate Tolerance Test (IPTT) to measure hepatic gluconeogenesis, and to assess pancreatic histology for routine histogical examination. In this experimental study, eight-teen male mice were assigned to three equal groups. Mice were divided by the saline injected group (control) and iron dextran injection 0.1 mg/mice (group 2) and 0.3 mg/mice (group 3) dose of injection. Iron dextran was injected daily intraperitoneally. After 14 days of treatment, IPGTT, IPTT and pancreas histology were examined. Repeated analysis of variance (ANOVA) with bonferroni's posthoc multiple comparison test were used for data analysis. IPGTT results showed glucose level was lower 39.85 % in group 3 compared to the control group mice. The results of IPTT showed that glucose level in mice treated with iron dextran were significantly lower in dose dependent manner. Pancreas histology showed islet cells in group 3 decreased in size, which might be due to beta cells depletion. Short term iron injection increases glucose tolerance and supresses hepatic gluconeogenesis in mice.

***Keywords* - Excess Iron, Glucose Metabolism Disorder, Intraperitoneal Glucose Tolerance Test (IPGTT), Intaperitoneal Pyruvate Tolerance Test (IPTT).**

1 INTRODUCTION

Iron is an essential element for synthesis of haemoglobin in the erythrocytes, cofactor for oxidation-reduction reactions, and cell proliferation. The average daily iron intake is 1-2 mg/day and the amount is strictly regulated to fit the body needs. Excess iron in the body can trigger pathological conditions through the production of reactive oxygen species (ROS) that cause organ dysfunction [1,2]. Excess iron accumulate in several organs including the heart, liver, and endocrine organs and can lead to serious problems such as cardiomyopathy, liver failure, and diabetes [1,3].

The first evidence for association of iron with human diabetes mellitus comes from clinical observations in individuals with pathologic iron overload e.g in patients with thalassemia who undergo transfusions on a regular basis to maintain the amount of erythrocytes. The prevalence of diabetes mellitus in thalassemia patients is 6 to 14% [4]. It is suggested that the cause of diabetes mellitus in β thalassemia major patients is due to iron accumulation in the liver which reduce the hepatic clearance of insulin that lead to hyperinsulinemia and insuline resistance. Over time, Insulin resistance will contribute to high-insulin-dependent pancreatic injury. Other than that, diabetes mellitus in β thalassemia major is also caused by pancreatic beta cell damage due to direct oxidant effects of iron accumulation in the pancreas [1,2,5,6]. The deposition of iron in the liver and pancreas can impair glucose tolerance and may progress to overt diabetes mellitus [7,8].

The condition of iron overload can disrupt glucose metabolism and cause hyperinsulinemia through decreased insulin extraction and insulin signaling [9,10]. Insulin has effect on increasing the synthesis of ferritin and redistributing of transferrin receptors (TfRs) in cells so that large amounts of iron can enter cells and tissues, decreasing the regulation of hepsidine expression in hepatocytes and adipocytes, stimulating expression of ferroportin, ferritin heavy chain