Molecular mechanisms involved in lead induced disruption of hepatic and pancreatic glucose metabolism

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ABSTRACT

Lead (Pb) is a toxic heavy metal known to be associated with pathology of various human chronic diseases. This study has focused on the effect of lead on glucose homeostasis with regard to metabolic function of pancreas and liver. Islets of Langerhans were isolated from the pancreas of rats and exposed to lead for 24 h, then insulin release along with markers of ER stress and oxidative stress were evaluated. In another part, lead was administered to rats for 32 days and after evaluating criteria of diabetes, the activity of gluconeogenesis and glycogenolysis enzymes, and markers of oxidative stress and inflammation were measured in the liver. Lead disrupted insulin secretory function of islets through activating GSK-3β and ER stress, and increased activity of gluconeogenic enzymes in the liver featured by glucose intolerance. Chronic exposure to lead can disrupt glucose homeostasis by affecting pancreas and liver mainly through induction of insulin resistance.

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1. Introduction

The heavy metal lead (Pb) is an abundant environmental toxicant with a wide range and long history of use dating back to Roman times. Despite wide toxicological studies, there is still debate on the hazards of lead for the general population through long time exposure to low levels of this toxicant in drinking water, food, and air (Karrari et al., 2012; Mehrpour et al., 2012). During the last decade, the exposure levels below...