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Effect of styrene exposure on plasma parameters, molecular mechanisms and gene expression in rat model islet cells.

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Abstract

Styrene is an aromatic hydrocarbon compound present in the environment and have primary exposure through plastic industry. The current study was designed to evaluate styrene-induced toxicity parameters in rat plasma fasting blood glucose (FBG) level, oral glucose tolerance, insulin secretion, oxidative stress, and inflammatory cytokines in cellular and molecular levels. Styrene was dissolved in corn oil and administered at different doses (250, 500, 1000, 1500, 2000mg/kg/day and control) to each rat, for 42days. In treated groups, styrene significantly increased fasting blood glucose, plasma insulin ($p < 0.001$) and glucose tolerance. **Glucose tolerance, insulin resistance and hyperglycemia were found to be the main consequences correlating gene expression of islet cells.** Styrene caused a significant enhancement of oxidative stress markers ($p < 0.001$) and inflammatory cytokines in a dose and concentration-dependent manner in plasma ($p < 0.001$). Moreover, the activities of caspase-3 and -9 of the islet cells were significantly up-regulated by this compound at 1500 and 2000mg/kg/day styrene administrated groups ($p < 0.001$). The relative fold change of GLUD1 was downregulated ($p < 0.05$) and upregulated at 1500 and 2000mg/kg, respectively ($p < 0.01$). The relative fold changes of GLUT2 were down regulated at 250 and 1000mg/kg and up regulated in 500, 1500 and 2000mg/kg doses of styrene ($p < 0.01$). The expression level of GCK indicated a significant upregulation at 250mg/kg and downregulation of relative fold changes in the remaining doses of styrene, except for no change at 2000mg/kg of styrene for GCK. Targeting genes (GLUD1, GLUT2 and GCK) of the pancreatic islet cells in styrene exposed groups, disrupted gluconeogenesis, glycogenolysis pathways and insulin secretory functions. **The present study illustrated that fasting blood glucose, insulin pathway, oxidative balance, inflammatory cytokines, cell viability and responsible genes of glucose metabolism are susceptible to styrene, which consequently lead to other abnormalities in various organs.**

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KEYWORDS: Gene expression; Glucose; Inflammatory cytokines; Insulin; Oxidative stress; Styrene

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