Abstract

Purpose

Benzene (C_6H_6) is the most commonly used industrial chemical, component of petroleum products and an environmental contaminant. The aim of this study was to examine the subchronic effect of benzene and its metabolite; hydroquinone, on liver and pancreas regarding glucose regulation in rat.

Methodology

In vivo part

Benzene was dissolved in corn oil and administered orally via gavage at doses of 200, 400 and 800 mg/kg/day, for 4 weeks. Liver and pancreas were used for assessing the toxic effects of benzene.

In vitro part

And, in the in vitro part, toxic mechanisms responsible for weakening the antioxidant system in islets of Langerhans by hydroquinone at different concentrations (0.25, 0.5 and 1 mM), were revealed.

Results

Benzene exposure raised the activity of phosphoenolpyruvate carboxykinase (PEPCK), glucose-6-phosphatase (G6Pase), in comparison to control. A significant increase was observed in hepatic tumor necrosis factor (TNF-α) in benzene-treated rats. The activity of hepatic glucokinase (GK) was decreased significantly. Moreover, benzene caused a significant rise in hepatic lipid peroxidation, DNA damage, and proteins oxidation. Benzene significantly raised the concentration of plasma insulin in comparison to control. Also the effect of benzene on the release of glucose-induced insulin was pronounced in islets. The level of DNA damage, lipid

peroxidation and reactive oxygen species (ROS) were found in islets of benzene exposed animals. All doses of benzene caused a significant rise in the level of 8-OHdG as an index of DNA damage in pancreatic islets and reduction in total thiols. In islets of Langerhans, hydroquinone was found to decrease the capability of antioxidant system to fight free radicals. Also, the level of death proteases (caspase 3 and caspase 9) were found high in hydroquinone exposed islets.

Conclusion

In conclusion, the present study indicates that repeated administration of benzene induces functional alterations in the liver and pancreas, as evident in the form of increased oxidative stress, change in the activity of gluconeogenic enzymes and rise in the level of TNF-α. Also, hydroquinone, a benzene metabolite, caused disruption, both in antioxidant system and enzymes of apoptosis. Decreasing the capability of the pancreatic antioxidant system and elevated level of oxidative stress along with marked alteration in the activity of gluconeogenic enzymes are indicative of benzene toxicity on the much regulated biochemical phenomenon of liver and pancreatic glucose metabolism. Nonetheless, the findings in the present study are preliminary, which in turn need comprehensive evaluation by recruiting more biochemical parameters with regard to glucose metabolism. Moreover, on the basis of current findings, we assumed that benzene has the potential to be further evaluated, both in experimental and epidemiological studies, with respect to diabetic toxicity.