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Hepatic Oxidative and Histological Changes in High Fat Diet and Streptozotocin-induced Diabetic Rats

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Background: An experimental animal model of type 2 diabetes mellitus (T2DM) facilitates the studying of antidiabetic and antioxidative effects of novel drugs. Feeding high-fat diet (HFD) followed by a low-dose streptozotocin (STZ) injection is used to induce diabetes and oxidative changes in the experimental animal model of diabetes.

Objectives: To investigate oxidative and histological changes in the liver of Wistar rats with T2DM.

Methods: Thirty Wistar rats were divided into five groups as group 1: healthy control, group 2: HFD control, group 3: HFD for four weeks + STZ (30 mg/kg, ip), group 4: HFD for four weeks + STZ (40 mg/kg, ip) and group 5: HFD for four weeks + STZ (50 mg/kg, ip). The liver tissues were excised from sacrificed animals in all groups and were used for the histological assessment and biochemical assessment of lipid peroxidation. Malondialdehyde (MDA) concentration in the liver homogenate was measured using thiobarbituric acid method to assess the level of lipid peroxidation. Liver tissues were stained in H&E and a semi-quantitative assessment was conducted to examine histological changes.

Results: The MDA concentration of the healthy control group, HFD control group, STZ-30, STZ-40 and STZ-50 mg/kg were 15.81 (± 2.09), 20.74 (± 1.97), 24.27 (± 6.20), 32.87 (± 1.13), 128.76 (± 14.89) nmol/protein (g), respectively. There was a significant increase in MDA concentration ($p < 0.05$) in STZ-40 and STZ-50 mg/kg groups compared to the healthy control group. The incidence of fatty degeneration, micro and macrovesicular changes, inflammatory infiltration, and other histological features of STZ induced diabetes mellitus were more pronounced in rats treated with the highest dose (50 mg/kg) of STZ. Accordingly, the highest mean histological score (10) was obtained for rats induced with the STZ-50 mg/kg.

Conclusions: STZ-induced oxidative stress, hepatocyte damage and changes in hepatic morphology were dependent on the dose of STZ. Histological findings corroborated the biochemical evidence of oxidative stress in high-fat fed low dose STZ induced diabetic rats.

Keywords: *High fat diet, Malondialdehyde, Oxidative stress, Streptozotocin, Type 2 diabetes mellitus*

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