The Cardioprotective Effect Of Human Glucagon-Like Peptide-1 Receptor Agonist (Semaglutide) on Cisplatin-Induced Cardiotoxicity in Rats: Targeting Mitochondrial Functions, Dynamics, Biogenesis, And Redox Status Pathways

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Abstract:

The cardiotoxic effect of chemotherapeutic agents as cisplatin has become a major issue recently. Interference with mitochondrial dynamics, biogenesis, redox status, and apoptosis are the most possible underlying mechanisms. Semaglutide is a human glucagon-like peptide-1 receptor agonist (GLP-1R), which is used primarily for the treatment of DM. Various recent studies have investigated (GLP-1R) role in cardiovascular diseases due to antiapoptotic and antioxidant effects. The current study aimed to investigate the curative role of semaglutide's against cisplatin induced cardiotoxicity and its relation to mitochondrial functions, dynamics, biogenesis, apoptosis, and redox status pathways.

The study included 30 male rats divided into three groups: control, cisplatin-induced cardiotoxicity, and cisplatin-induced cardiotoxicity treated with semaglutide. At the end of the experiment heart index, serum cardiotoxicity markers, SOD, GPX activities and H_2O_2 level were estimated. Mitochondrial transmembrane potential, complex I and citrate synthase enzyme activities, ATP level, Mfn2 in addition to PGC-1 α levels were assessed as biogenesis markers. Mitophagy markers PINK1 and Parkin mRNA gene expression were estimated. Histopathological examination of cardiac muscles of all studied groups and immunoassay of P53 and caspase 3 in cardiac tissue were examined to assess apoptosis. Cisplatin has disturbed mitochondrial function and dynamics, dysregulate redox status and induced mitophagy and apoptosis, in the other hand semaglutide treatment has normalized dysregulated mitochondrial function and dynamics, redox status and suppressed mitophagy and apoptosis.

Semaglutide has ameliorative effect against cisplatin- induced cardiotoxicity via modulation of mitochondrial functions, dynamics, biogenesis, apoptosis, and redox status pathways.