

Paper Two

Assessment of the cardioprotective effect of liraglutide on methotrexate induced cardiac dysfunction through suppression of inflammation and enhancement of angiogenesis in rats.

Abstract: Methotrexate (MTX) is one of the most commonly used anti-cancer drugs for various types of neoplasms. It is associated with multiple cytotoxic effects including nephrotoxicity, hepatotoxicity and cardiotoxicity. Liraglutide (LIR) is a potent anti-diabetic drug and also has antioxidant and anti-inflammatory properties. In this study, we tried to investigate the protective effect of LIR on MTX induced cardiotoxicity and to identify the molecular mechanisms for this protection. Rats were divided into 4 groups, including control group, LIR group, MTX group and LIR + MTX group. ECG was measured then blood samples were taken, and hearts were excised for biochemical and histological investigations.

MTX group exhibited a mild non-significant irregular bradycardia, an increase of CK-MB besides a decrease of total antioxidant capacity. MTX administration also resulted in downregulation of vascular endothelial growth factor (VEGF), while caused upregulation of interleukin 1 beta (IL-1B) and interleukin 6 (IL-6) in comparison to the control group. Also, MTX group showed histological abnormalities besides negative VEGF and positive iNOS as detected by immunohistochemical staining compared to the control group. LIR administration could reverse these results. LIR prevented MTX induced cardiotoxicity through its antioxidant and anti-inflammatory properties.