البحث السابع

Modulation of cardio-metabolic disorders by Tocilizumab in rats with fructose – induced metabolic syndrome: Role of cardiac NLRP3 inflammasome and TIMP1"

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Abstract

Introduction: Insufficient regulation of NLRP3 inflammasome and TIMP1 has a role in the pathogenesis of CVD. Moreover, tocilizumab has a cardio-metabolic protective effect mainly through improved metabolic indices, IL6, alongside cardiac TNFα, NLRP3, and TIMP1 activity.

Aim of the study: The study aims to examine the effect of IL6 receptor blocker; tocilizumab on cardiovascular disorders (CVD) in rats with fructose-induced metabolic syndrome (MetS); elucidating how it works.

Subjects and Methods: Four groups of male albino rats were allocated into Control, Tocilozumab (8mg/kg/week intraperitoneal), Fructose (10-25%in drinking water), and Fructose+Tocilizumab. After seven weeks of the experiment, measurements of systolic blood pressure (SBP), heart rate (HR), serum fasting glucose, insulin, lipids, IL6 levels, and HOMA test for insulin resistance (IR) were done. Cardiac tissue concentrations of nucleotide-like receptor protein 3(NLRP3) inflammasome and tissue inhibitor metalloproteinase1 (TIMP1) were estimated. Finally, a histopathological heart examination was performed.

Results: Treatment with tocilizumab significantly alleviated the fructose–induced metabolic disorders such as increased HR, glycemic parameters, IR, lipid profile, and IL6. Concurrently, tocilizumab ameliorated cardiac NLRP3 and TIMP1 concentrations; normalizing the histopathological findings of inflammatory infiltration, interstitial fibrosis, and TNFα immunohistological reactivity.

Conclusions: These results show promising cardiovascular protective effects of tocilizumab to be used clinically. However, further cardiovascular investigations such as ventricular contractility, ECG, and vascular reactivity may be required to interpret more benefits of tocilizumab for this purpose.

Keywords: Fructose, IL6, inflammasome, TIMP1, Tocilizumab.