ABSTRACT

Aras, M. (2026). Evaluation of the Cardiovascular Effects of the GLP-1 Receptor Agonist Semaglutide in a Rat Model of Type 2 Diabetes Mellitus. İstanbul University, Institute of Health Science, Faculty of Pharmacy, Department of Pharmacology. PhD Thesis. İstanbul.

Semaglutide is a long-acting GLP-1 receptor agonist approved for the treatment of obesity and type 2 diabetes mellitus (T2DM). Although semaglutide improves glycemic control and promotes weight loss, its cardiovascular effects and the mechanisms underlying its cardioprotective potential in T2DM remain incompletely understood. This study aimed to evaluate the possible cardiometabolic and cardioprotective effects of semaglutide in an experimental rat model of T2DM. Experimental T2DM was induced in male Wistar rats using a high-fat high-fructose diet combined with low-dose streptozotocin (HFHFD/STZ). Semaglutide was administered intraperitoneally at doses of 0.15, 0.3, and 0.6 mg/kg for 6 weeks. At week 15, body weight, food and water intake, and fasting blood glucose levels were assessed. After sacrifice, plasma insulin, total cholesterol, and triglyceride levels were measured. Adiponectin, leptin, omentin, and TNF-α levels were also determined in plasma and perivascular adipose tissue (PVAT). Isolated hearts were subjected to 30 min global ischemia followed by 60 min reperfusion in the Langendorff system, and cardiac functional parameters were recorded. CK-MB and troponin-T levels were measured in the perfusate, while MDA and SOD levels were evaluated in heart tissue. Heart, liver, thoracic aorta, and PVAT were examined histopathologically. Semaglutide improved body weight and cardiometabolic parameters in experimental T2DM. It also favourably modulated adipocytokine profiles in plasma and PVAT. Although cardiac functional parameters were not markedly altered, reduced myocardial injury and oxidative stress markers supported its cardioprotective potential. Partial histopathological improvements in heart and liver tissues further strengthened this profile of effects. Consequently, semaglutide ameliorates diabetic cardiometabolic dysfunction.

Key Words: Type 2 diabetes mellitus, glucagon-like peptide-1, semaglutide, myocardial ischemia/reperfusion, perivascular adipose tissue

The present work was supported by the Research Fund of Istanbul University. Project No:40100