Effect of Sacubitril /Valsartan and Liraglutide on cardiac dysfunction, N-terminal pro brain natriuretic peptide and Rho-associated protein in deoxycorticosterone induced hypertension in Rats

Thesis

Submitted in partial fulfillment of the

Requirement for the degree of MSc in clinical Pharmacology

By

Dina Sayed Abd El-Salam

M.B.B.Ch
Demonstrator of clinical Pharmacology
Faculty of Medicine- Fayoum University

Supervised by

Professor Sawsan Abd El-Aziz Sadik
Professor of clinical Pharmacology
Faculty of Medicine - Fayoum University

Professor Nawal El- Sayed El-Gawhary
Professor of clinical Pharmacology
Faculty of Medicine- Cairo University

Dr. Eman Sayed Said
Lecturer of clinical pharmacology
Faculty of Medicine-Fayoum University

Faculty of Medicine
Fayoum University
2022

ABSTRACT

The aim of the present work is to highlight the potential protective effect of sacubitril/valsartan and liraglutide on cardiac dysfunction in DOCA induced hypertension in rats.

Hypertension was induced in male albino rats by injection of DOCA 50 mg/kg once/week SC in 0.3 ml olive oil and NaCl (1%) in drinking water for 3 weeks. Rats were divided into six groups: three control groups (normal, sacubitril/valsartan and liraglutide control), and three hypertensive groups (DOCA, DOCA+sacubitril/valsartan and DOCA+liraglutide).

Sacubitril/valsartan 60 mg/kg/day orally, and liraglutide 0.3 mg/kg/day SC for 3 weeks were administered to study their effects on blood pressure (systolic, diastolic and mean arterial pressure), heart rate, body weight, blood glucose, serum N-terminal pro brain natriuretic peptide (NT pro BNP) and serum (ROCK1) in deoxycorticosterone (DOCA) salt hypertensive rats. Histopathological analysis of cardiac tissue was also performed.

The present study revealed that DOCA induced hypertension led to significant increase in SBP, DBP and MAP by 66.8%, 39.3% and 50.8% respectively and significant decrease in heart rate by 10.2%.

The present work proved that sacubitril/valsartan treatment significantly decreased SBP, DBP and MAP by 18.3%, 16.2% and 17.3% respectively, while liraglutide significantly decreased SBP, DBP and MAP by 13.8%, 14.6% and 14.3% respectively. As regards the heart rate,

sacubitril/valsartan significantly increased heart rate by 9.2% while the heart rate is significantly increased by 11.2% with liraglutide.

DOCA led to a significant increase in blood glucose level by 26.8%. Treatment with sacubitril/valsartan significantly decreased blood glucose level by 17.9% while liraglutide treatment significantly decreased blood glucose by 34.4%.

DOCA induced hypertension led to a significant increase in serum NT pro BNP by 34%. Sacubitril/valsartan significantly decreased NT pro BNP by 22.8% and liraglutide decreased it by 10.1%.

Serum Rho- kinase (ROCK1) enzyme was increased significantly in DOCA hypertensive group by 49.7%. Treatment with Sacubitril/valsartan and liraglutide significantly decreased serum ROCK1 by 15.5% and 24.4% respectively.

Histopathological examination by light microscopy using hematoxylin and eosin revealed irregular arrangement, marked connective tissue, congestion, and inflammatory cells in DOCA group. Sections stained by Masson's trichrome showed marked interstitial fibrosis in the DOCA group which was ameliorated with sacubitril/valsartan and to a lesser extent with liraglutide treatment.

Key words: DOCA, hypertension, NT pro BNP, ROCK1, Sacubitril/valsartan and liraglutide