

Effect of Fasudil, Dulaglutide and Ivabradine on cardiac dysfunction in rats with experimental metabolic syndrome

Thesis

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By

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SUMMARY

Metabolic syndrome represents a clustering of cardiovascular risk factors that include abdominal obesity, dyslipidemia, insulin resistance and hypertension. Sucrose is a dietary source of fructose. Thus sucrose feeding has been used to induce metabolic syndrome in animal models

The present study demonstrates the effect of fasudil(a potent Rho-kinase inhibitor) dulaglutide (glucagon-like peptide-1 receptor agonist(GLP-1RA) and ivabradine (a hyperpolarization activated cyclic nucleotide-gated channel blocker that blocks If current , which regulates pacemaker activity on cardiovascular dysfunction in sucrose-induced metabolic syndrome in rats

:Experimental Design

In this study, rats were divided into 8 groups each containing 6 rats

:(Group 1 (Control group

.Rats received distilled water orally for 3 weeks

:(Group 2 (Fasudil group

Rats were given subcutaneous fasudil (10 mg/ kg) daily for 3 weeks

:(Group 3 (Dulaglutide group

Rats were given subcutaneous injection of dulaglutide (0.626mg/kg) twice weekly for 3 weeks

‡(Group 4 (Ivabradine group

.Rats were given oral ivabradine (10 mg/kg) daily for 3 weeks

:(Group 5 (Sucrose fed group

. Rats were given sucrose (30%) in drinking water for 3 week

‡(Group 6 (Sucrose + Fasudil group

Rats were given sucrose (30 %) in drinking water and given

.subcutaneous injection of fasudil (10 mg/ kg) daily for 3 weeks

‡(Group 7 (Sucrose + Dulaglutide group

Rats were given sucrose (30 %) in drinking water and given

subcutaneous injection of dulaglutide (0.626mg/kg) twice weekly for 3

.weeks

‡(Group 8 (Sucrose + Ivabradine group

Rats were given sucrose (30%) in drinking water and given oral

.ivabradine (10 mg/kg) daily for 3 weeks

At the end of the three weeks, animals were fasted for 12 hours

and the following parameters were investigated BP, heart rate , serum

glucose , serum insulin ,HbA1C, Rho kinase, serum LDL and nitric

.oxide

Rats were sacrificed by cervical dislocation and hearts were

excised .After that hearts were washed with ice-cold saline and preserved

for estimation of Brain natriuretic peptide (BNP) and Proprotein

convertase subtilisin / kexin type 9 (PCSK9) by enzyme-linked

.(immunosorbent assay (ELISA

Results revealed that SBP, heart rate and body weight were significantly decreased with treated groups compared to sucrose groups

We found also significant increase in serum glucose and HbA1C with sucrose group compared with control groups and significant decrease in treated groups compared with sucrose group

Also there was significant decrease in LDL, NO, Rho and PCSK9 with treated groups compared with sucrose group but we found significant increase in BNP with treated groups compared with sucrose group

Histopathological examination using H& E revealed no abnormal microscopy for the cardiac muscles of the four control groups. In sucrose group myocytes appeared hypertrophied but with no vacuolation of cytoplasm and with mild interstitial fibrosis in Masson trichrome stained sections. Hypertrophy of the myocytes was markedly decreased in all treated groups meanwhile the interstitial fibrosis was markedly decreased in treated groups compared to sucrose groups.