Canagliflozin Reveals a Cardioprotective Effect in Acute Myocardial Infarction Management via Modulation of WnT/ β-catenin Pathway

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Background:

Canagliflozin (CANA) is an antidiabetic drug of sodium-glucose co-transporter 2 inhibitor (SGLT2i) group. CANA was reported to reduce pathological events associated with heart failure. However, the exact mechanism by which CANA positively acts on cardiac tissue requires further elucidation.

Aim and objectives:

The current study aimed to investigate the effects of CANA, and/or carvedilol (CRV) on acute myocardial infarction (AMI) induced experimentally.

Methods:

Fifty male albino rats were assigned to five groups. AMI was induced by SC injection of 85 mg/kg isoproterenol on 2 consecutive days in all rats except the normal group. Three groups of AMI were treated orally by CANA and/or CRV for 7 days. Rats were anesthetized, blood was collected and serum was used for measuring cardiac troponin I (cTnI), malondialdehyde (MDA)and total antioxidant capacity(TAC)levels. Hearts were excised, portions were used for assay of Wnt/β-catenin, autophagy-related protein5(Atg5), tumor necrosis factor- α (TNF-α), and caspase-3 for histopathological examination. levels. The remaining portions were fixed in formalin

Result:

AMI untreated group exhibited elevation in cTn-I, MDA, TNF-α, WnT, β-catenin, and caspase-3 together with reduction in TAC and Atg5 levels. Histopathological studies revealing distorted cardiomyocytes, necrosis, areas of hemorrhage, and mononuclear cellular infiltration. Either CRV or CANA ameliorated all the toxicity indicators with a pronounced improvement observed in the combination-treated group.

Conclusion:

Combined CRV + CANA revealed efficient ameliorative actions against isoproterenol-induced MI by a marked reduction in cardiac enzymes, suppression of oxidative stress, inflammation, and apoptosis with increased antioxidants and activation of autophagy via downregulation of Wnt/ β-catenin pathways.

Keywords:

Acute myocardial infarction, Canagliflozin, Wnt/ β-catenin.