البحث السادس

" Fasudil, a Rho kinase inhibitor, attenuates cardiovascular disorders in an experimental rat model of metabolic syndrome via modulation of PCSK9 and BNP."

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Abstract

OBJECTIVE Metabolic syndrome (MS) is an important cardiovascular risk factor. Rho-kinase(ROCK) is a novel cardiovascular therapeutic target and its activity is increased in patientswith MS.The study's objective was to investigate the impact of fausdil, a Rho kinase inhibitor, on the Rho-ROCK pathway , nitric oxide (NO), brain natriuretic peptide(BNP) and cardiac PCSK9/LDL concentrations, and to explore its potential role in improving insulin resistance and cardiovascular abnormalities.

MATERIALS AND METHODS: 24 adult male Wistar albino rats were used and divided into 4 groups: Control, Fasudil (10 mg/kg /day subcutaneously), Sucrose-fed(30% in drinking water) Sucrose+Fasudil group daily for 3 weeks. Blood pressure and heart rate, serum biomarkers (ROCK1,BNP, NO, insulin, glucose and LDL-c) , and cardiac PCSK-9 concentrations were assessed in addition to cardiac histopathology.

RESULTS: The data proved that sucrose + fasudil treatment significantly ameliorated the levels ofsystolic blood pressure, glycemic indices, serum LDL, Rho kinase, NO, and BNP and cardiac PCSK9compared to the untreated sucrose group. Histology examination confirmed the positive impact of fasudil on cardiac inflammation, fibrosis and tissue degeneration compared to the untreated.

CONCLUSION: Fasudil has a cardioprotective effects with improved glycemic indices on sucrose-induced MS in rats. By its action not only on RhoA/Rho kinase (ROCK) signaling pathway but also onBNP, NO, and cardiac PCSK9 modulation activity.The study provided a promise to use fasudil clinically in MS beyond RhoA/ROCK inhibtiton.

Keyword: Fasudil, Sucrose, PCSK9, BNP.