Rita Zilinyi, J Cardiovasc Dis Diagn 2019, Volume 7
DOI: 10.4172/2329-9517-C1-017

The cardioprotective effect of Metformin on Doxorubicin-induced cardiotoxicity

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Introduction: Doxorubicin (DOX) is an effective chemotherapeutic agent, but its cardiotoxicity has been an important clinical limitation. However, the complex molecular mechanisms underlying DOX-induced cardiac damages are still being uncovered, but known to involve, mitochondrial dysfunction, oxidative stress, lipidperoxidation and apoptosis. Recently, a number of studies have investigated the role of autophagy on DOX-induced cardiotoxicity but to date it is not clear how DOX alters that process and its consequence on cardiomyocytes.

Aim: The aim of our study was to investigate the possible protective role of Metformin (MET) and its effect on autophagy in a model of DOX-induced cardiotoxicity.

Methods: Female Sprague-Dawley rats were segregated into four groups and animals were treated with (1) vehicle (Control group), (2) Doxorubicin (3 mg/kg every second day) intraperitoneally (DOX group), (3) Metformin (250 mg/kg/day) (MET group), (4) Doxorubicin+Metformin (both at the before-mentioned dose) (DOX+MET group) for two weeks. After the last dose of DOX isolated working hearts were prepared and heart function parameters were evaluated. Serum level of LDH, CK-MB enzymes and cardiac Troponin-T were measured. To investigate the degree of lipidperoxidation cardiac Malondialdehyde (MDA) level was evaluated. To monitor the morphological changes in the heart tissue Masson's trichrome staining was carried out. To evaluate the different autophagy-related markers expression level in the left ventricular tissue including AMPK, beclin-1, LC3B-II and p62, we conducted Western blot analysis.

Results: Our results revealed that MET produced elevated cardiac protection manifested by remarkable improvement in heart functions, significant decrease in serum Troponin-T, notable reduction in the level of cardiac MDA and significant meliorism in histopathological features. Moreover, by focusing on the autophagic markers, we have found that MET restored the autophagic process and increased the expression of AMPK, which may serve as a survival pathway for cardiomyocytes during DOX treatment.

Conclusion: Taken together these results may suggest administering MET for patients receiving DOX would be preferable drug and may help to reduce the irreversible side effects of DOX.

Biography

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