Cardioprotective Effect of Metformin Against Doxorubicin Cardiotoxicity in Rats


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Introduction:
The clinical use of doxorubicin, which is a strong antineoplastic agent, is limited due to its cardiotoxic side effects. Metformin is a drug with anti-hyperglycemic effects, and it has been shown to have a cardioprotective effect on left ventricular function in experimental animal models of myocardial ischemia. The present study investigated the cardioprotective effect of metformin in rats with doxorubicin cardiotoxicity.

Methods:
Forty male, 10-week-old Wistar albino rats were randomly divided into four groups. The control group rats were intraperitoneally administered saline solution twice a week, four doses in total. The doxorubicin group rats received (cumulative dose: 16 mg/kg) intraperitoneally. The metformin group rats received metformin with gavage. The doxorubicin + metformin group rats received doxorubicin (cumulative dose: 16 mg/kg) intraperitoneally and metformin orally with gavage.

Left ventricular functions were evaluated by using M-mode echocardiography one day after the last dose of doxorubicin. Heart tissue samples were histopathologically examined. Cardiomyocyte apoptosis was detected using in situ terminal deoxynucleotide transferase assay (TUNEL). Serum brain natriuretic peptide and C-type natriuretic peptide levels were measured. Catalase, superoxide dismutase, glutathione peroxidase, and tumor necrosis factor alpha levels were analyzed in the heart tissue.

Results:
Our results showed that doxorubicin treatment caused significant deterioration in left ventricular function by echocardiography, histological heart tissue damage, and increase in cardiomyocyte apoptosis. The while, doxorubicin + metformin group showed protection in left ventricular function, inhibition of cardiomyocyte apoptosis (Figure).

![Figure 1](image1.jpg)

Figure 1 M-mode left ventricle echocardiography examination in experimental groups. (a; control group, b; doxorubicin group, c; metformin group, d; doxorubicin + metformin group).

Conclusion:
The present study provided evidence that metformin has cardioprotective effects against doxorubicin cardiotoxicity.