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Renin inhibition alleviates doxorubicin-induced nephrotoxicity by inhibiting oxidative stress and podocyte injury

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Objectives : This study aimed to investigate the possible protective effects of aliskiren against doxorubicin (DXR)-induced cardiorenal injury and to identify the mechanisms involved

Methods : Albino rats of Wistar strain, with body weight 160–200 g were used. Animals were acclimatized under standard laboratory conditions at 20–25 °C. After acclimatization, rats were allocated into seven groups consisting of eight animals each. Group I served as vehicle control and received phosphate buffer solution (1 mL/kg/day, orally) for 14 days. Group II served as DXR control and received single acute dose of DXR (15 mg/kg, intraperitoneally), on 10th day of the treatment. Groups III, IV, V, and VI received ALK 30, ALK 50, ALK 100, and TEL 10 mg/kg/day, by oral route, respectively, for 14 days along with single acute dose of DXR (15 mg/kg, intraperitoneally), same as group II. Group VII served as per se and received ALK alone (100 mg/kg/day, orally.) for 14 days. Blood samples were withdrawn from tail vein at 14th day of treatment for the estimation of LDH, albumin, total protein, angiotensin I, blood urea nitrogen (BUN), and creatinine. Heart and kidney tissue were preserved for ultrastructural studies.

Results : Oral administration of aliskiren (100 mg/kg, for a period of 14 days) significantly prevented all the DXR-induced adverse effects and maintained the rats near to normal status. However, telmisartan (10 mg/kg) pretreatment has shown slight protection in DXR-induced renal injury as evidenced by broadening of podocyte foot process and narrowing of slit pore diameter. The results of aliskiren were compared with telmisartan which was used as reference in this study. These results suggested that aliskiren has protective effects against acute model of DXR-induced cardiotoxicity and nephrotoxicity, Implying that plasma renin activity plays a role in DXR-induced cardio-renal injury.

Conclusions : In conclusion, the results indicate that DXR induced cardiomyopathy and nephropathy have some RAS component. ALK is beneficial

in attenuating DXRinduced cardiac and renal damages in rats.

Keywords : Aliskiren; Nephrotoxicity; Renin