Cisplatin-induced cardiotoxicity: Mechanisms and cardioprotective strategies

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Abstract:
Increased oxidative stress and apoptosis have been implicated in the cardiotoxicity that limits the clinical use of cisplatin as an anti-tumoral drug. Our study was conducted to evaluate the protective potential of acetyl-L-carnitine, DL-α-lipoic acid and silymarin against cisplatin-induced myocardial injury. Eighty male albino rats were divided into eight groups. The first four groups were treated with normal saline, acetyl-L-carnitine (500 mg/kg, i.p.), DL-α-lipoic acid (100 mg/kg, p.o.) and silymarin (100 mg/kg, p.o.) respectively, for 10 successive days. The remaining groups were treated with the same doses of normal saline, acetyl-L-carnitine, DL-α-lipoic acid and silymarin, respectively, for 5 successive days before and after a single dose of cisplatin (10 mg/kg, i.p.). Serum activities of lactate dehydrogenase (LDH), creatine kinase (CK), creatine kinase isoenzyme MB (CK-MB) and plasma cardiac troponin I (cTnI) concentration were estimated. Malondialdehyde (MDA), reduced glutathione (GSH) contents, superoxide dismutase activity (SOD) and protein content in cardiac tissues were measured. Moreover, integrity of both mitochondrial DNA (mtDNA) and nuclear DNA (nDNA) was also examined. Cisplatin-treated rats experienced a significant elevation of serum activities of LDH, CK, CK-MB and cTnI plasma concentration. These effects were accompanied by a significant increase in MDA level. On the other hand, a significant decrease in GSH content, SOD activity and total protein content was observed. In addition, both mtDNA and nDNA were heavily damaged. However, acetyl-L-carnitine, DL-α-lipoic acid and silymarin significantly attenuated the cisplatin-evoked disturbances in the above-mentioned parameters. In conclusion, the former drugs were proven to be potential candidates to ameliorate cisplatin-induced cardiotoxicity.