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Protective effect of tetrandrine on doxorubicin-induced cardiotoxicity in rats

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ABSTRACT

Aims and background. Doxorubicin (Dox) is effective in curative and adjuvant chemotherapy of malignant tumors. Cardiotoxicity is the chief toxic effect that limits the clinical use of Dox. We studied the effects of tetrandrine (Tet) on doxorubicin-induced cardiotoxicity in rats and its protective activity.

Materials and methods. Sprague-Dawley rats were randomly divided into the following 4 groups: a control group (received only saline), Dox group (received only Dox), Tet/Dox group (received Tet plus Dox), and Tet group (received only Tet). Rats were injected intravenously with 2 mg/kg Dox once a week for 7 weeks and 50 mg/kg Tet was administered intraperitoneally weekly for 7 weeks. Measurements of cardiac contractile parameters including LSVP, +dP/dt max and -dP/dt max, and assessment of electrocardiograms were carried out. Mitochondrial oxidation and phosphorylation state 3 (S_3) and state 4 (S_4) respiration were measured. Respiration control rate (RCR) and the ADP/O ratio were calculated. Cardiac ultrastructure was examined by electron microscopy.

Results. Dox induced significant cardiotoxicity in this rat model. The values of LSVP, +dP/dt max, and -dP/dt max in the Tet/Dox group increased as compared to the Dox group (P <0.05). The cardiac contraction and relaxation improved on Tet administration. Tet inhibited the prolonged QT interval on the electrocardiogram in Dox-treated rats. Compared to the Dox group, the values of S_3, RCR, and ADP/O increased by more than 28%, 48%, and 27%, respectively, in the Tet/Dox group. Significant cardiac morphological protection was observed in the Tet/Dox-treated rats.

Conclusion. Tet can improve the reduced cardiac function caused by Dox treatment and prevent Dox-induced mitochondrial impairment in rat cardiotoxicity. Free full text available at www.tumorionline.it

Key words: doxorubicin, cardiotoxicity, oxidative phosphorylation, tetrandrine.

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