Taurine blunts doxorubicin cardiotoxicity: chronic and acute effects

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Aim. To study the functional statement of the isolated heart inherent to doxorubicin cardiotoxicity under the chronic and acute action of taurine.

Material and methods. Doxorubicin (Dx) cardiotoxicity manifested by heart failure development was reproduced classically by anthracycline i/p administration in rats in cumulative dose of 16 mg/kg (4 mg/kg four times during 2 weeks) – Dx series. Series with chronic action of taurine (Tr) included rats receiving this aminoacid daily per os during Dx administration (100 mg/kg) – Dx + Tr series. Rats of both series were sacrificed by euthanasia and the isolated heart was perfused by Krebs solution according to Langendorff (isovolumic heart) and Neely-Rovetto (working heart) methods in conditions of diverse hemodynamic and neuroendocrine efforts applying. Acute action of taurine was studied during its infusion in the perfusate of isolated hearts in final concentration of 40 μM. The hearts of intact rats constituted the control series.

Results. Chronic action of taurine has identified certain important functional benefits, the most important being underlined beneath. The first, taurine reversed the negative inotropic effect of isolated heart on endothelin-1 (ET-1) action (10-7 M), detected in Dx series and manifested by both systolic pressure of left ventricle (LV) and cardiac output fall by about 9,1%. Taurine assured increase of these indices during ET-1 stimulation. The second, Tr notably improved both isovolumic relaxation and contraction of myocardium exhibited by significant enhancement of Veragut index (118,6 ± 9,6 vs 94,8 ± 6,5 1/sec), +dP/dPmax (8389 ± 445 vs 7216 ± 363 mm Hg/sec) and -dP/dTmax (7526 ± 378 vs 5684 ± 322 mm Hg/sec) during efforts with volume and resistance. The third, Tr significantly decreased LV end diastolic pressure (LVSDP) when coronary pressure of isovolumic heart elevated by 50% (from 80 up to 120 cm H20 column): 16,2 ± 1,2 vs 18,8 ± 1,4 mm Hg. Acute Tr action manifested by: (i) significant LVSDP diminution during 30 min of ischemia (52,4 ± 3,1 vs 63,7 ± 4,4 mm Hg) and on 45th min of reperfusion (18,3 ± 1,3 vs 22,8 ± 1,4 mm Hg), (ii) increased time of LV extrasystole appearance when the glucose content of Krebs solution was reduced by 50% (28,6 ± 2,8 vs 22,5 ± 2,4 min), and (iii) increased time of LV tachyarrhythmia appearance when the potassium content of Krebs solution raised up to 6,5 meq/L (9,2 ± 0,5 vs 6,9 ± 0,3 min).

Conclusion. Taurine, a natural calcium modulator of the heart, notably improves functional reserves of the myocardium exposed to cardiotoxic action of Dx, and could be seen as a relevant remedy of primary and secondary prophylaxis of Dx induced heart failure in oncologic patients.