Amifostine improves hemodynamic parameters in doxorubicin-pretreated rabbits

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Abstract:
Amifostine reduces nephrotoxicity and myelotoxicity of alkylating agents. Little is known about its role in preventing cardiotoxicity. We studied if amifostine could affect the hemodynamic parameters in doxorubicin-pretreated rabbits. The animals were divided into six groups consisting of 6 rabbits each. Group 1 – doxorubicin iv 2 mg/kg of body weight 4 times every 14 days (cumulative dose 8 mg/kg); group 2 – a dose of doxorubicin was 3 mg/kg (cumulative dose 12 mg/kg); groups 3 and 4 – amifostine iv 30 mg/kg 15 min prior to doxorubicin 2 and 3 mg/kg, respectively, groups 5 and 6 – amifostine- and physiological saline-treated controls. Two-three weeks after the last dose the animals were anesthetized and cardiac index (CI) i.e. cardiac output/body weight, and total peripheral resistance (TPR) were calculated using the method of human I albumin dilution. Mean CI was 71.4 ± 40.5 ml/min/kg in group 2, 135.8 ± 41.2 in group 5 (p < 0.001), and 116.4 ± 47.8 in group 6 (p < 0.001), TPR was 4.7 ± 3.3 kPa × s/l, 1.1 ± 1.2 (p < 0.001), and 1.9 ± 1.1 (p < 0.001), respectively. In group 4, CI was 135.4 ± 33.2, and TPR was 1.1 ± 0.6. The differences in CI and TPR between groups 2 and 4 were statistically significant (p < 0.001). In conclusion, pretreatment with doxorubicin at the total dose of 12 mg/kg significantly reduced CI and increased TPR. Amifostine improved CI and TPR in doxorubicin-pretreated rabbits.

Key words:
doxorubicin, cardiotoxicity, amifostine, rabbits