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Spin-labelled 1-ethyl-1-nitrosourea prevents Doxorubicin and Bleomycin-induced oxidative stress in lungs, hearts and kidneys of tumour-bearing mice

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Administration of antineoplastic agents during cancer chemotherapy results in a much greater degree of oxidative stress than is induced by cancer itself. The purpose of this study was to investigate the effect of chemotherapy on some biomarkers of oxidative stress, such as: the stable products of free radical damage of lipids (MDA levels), proteins (Protein Carbonyl level) and nucleic acids (8-OHdG levels); the "Real time" Electron Paramagnetic Resonance (EPR) free radical formation of Nitric oxide NO• and Ascorbate radicals (Asc•) and the activities of the antioxidant enzymes, superoxide dismutase (SOD) and catalase (CAT)in patients with lymphoproliferative and myeloproliferative diseases.The investigated biomarkers of oxidative stress were found to be significantly changed in comparison to the control group for patients treated with the protocols CVP (cyclophosphamide, vincristine, prednisolon) and ABVD (adriamicine, bleomicine, vinblastine, dacarbasine). Erythrocyte enzymes SOD and CAT activities were statistically increased in patients treated with CVP and ABVD. In biggest risk of oxidative injury actually are patients with polychemotherapy of CVP and ABVD. Later, the possible protective effect of 1-ethyl-3-[4-(2, 2, 6, 6-tetramethylpiperidine-1-oxyl)]-1-nitrosourea (SLENU), recently synthesized in our laboratory on doxorubicin (DOX) and bleomycin (BLM)-induced oxidative toxicity in C57 black tumour-bearing mice. Specifically, alterations in biomarkers of oxidative stress were studied in lung, heart and kidney homogenates isolated from C57 black tumor-bearing mice after i.p. treatment with solutions of DOX (60 mg/kg) and BLM (60 mg/kg). The same biomarkers were also measured after i.p. pretreatment of mice with SLENU (100 mg/kg). After treatment with DOX, heart and kidney homogenates of mice had significantly higher stable products of free radical damage of lipids, proteins and nucleic acids compared to lung homogenates. It was accompanied by increased activity of the antioxidant defense enzyme SOD and decreased activity of CAT. Bleomycin-induced oxidative stress was confirmed by significantly higher production of stable products of free radical damage of lipids, proteins and nucleic acids in lungs compared to heart homogenates, elevation of the antioxidant activity of superoxide dismutase and decreased activity of catalase enzymes. After pretreatment of the mice with SLENU, the levels of all studied oxidative stress biomarkers were significantly improved in comparison with those of the mice treated alone with either bleomycin, or doxorubicin. The present results and those from a previously demonstrated superoxide scavenging activities (SSA) of the nitrosourea SLENU have enabled us to explain the protective effect of the spin-labelled nitrosourea on doxorubicin and bleomycin-induced oxidative stress by scavenging of · O2– and increased ·NO release.

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