Dose-rate Effects are Dependent on Cell Lines

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Background: A number of studies, including our own, have indicated that low dose rate of ionizing radiation might be (within some range) more effective in killing cells than high dose rate. This phenomenon is defined as "inverse dose-rate effect" and is mediated mainly by post radiation oxidative reactions, as radiation peroxidative damage increases with decreased dose rate. Knowledge of biological dose rate-dependent effects might have influence upon the extension of therapeutic maneuvers and limitation of normal tissue reaction. Aim: The aim of the present study was to evaluate the dose-rate effects on lymphoblastic cells since this type of cells is a target in total body irradiation. Materials and methods: Lymphoblastic K562 cells were exposed to 2 Gy X-ray dose (using a 6 MeV accelerator for therapeutic purposes), at high dose rate (2Gy/min), low dose rate (0.07 Gy/min) and at high dose rate, but total dose was given as short separated pulses delivered during the same time as low dose rate (28 min 34 sec). Cells were suspended in RPMI medium supplemented with serum and irradiated in culture flasks. After irradiation cells were incubated for 0.5 - 60 h and micronuclei, apoptotic, necrotic and mitotic cells were scored under fluorescent microscope. Activity of superoxide dismutase isoenzymes (MnSOD and CuZuSOD), and glutathione peroxidise as well as end-product of lipid peroxidation (malondialdehyde) were also measured. Results and discussion: Our results indicated that 2 Gy dose at high dose rate induced higher yield of micronuclei than the same dose at low dose rate or 2 Gy dose given in many pulses. At the same time high dose-rate was less effective in apoptosis induction in K562 cells than low dose-rate or pulsed dose. This effect may differ in different cell lines, since our study on murine carcinoma AT478 cells indicated opposite trend. Furthermore, there was no dose-rate effect in the activation of antioxidant enzymes in lymphoblastic cells, whereas inverse dose rate effect was observed for carcinoma cells. The observed differences may also result from the type of cell growth, K562 grow in suspension, but AT478 are adherent cells. The adherent cells may suffer higher damage from low dose rate during long time of irradiation, in part due to bystander effects. The ongoing study is aimed at evaluating the mechanisms responsible for observed differences and possible signalling activated at different dose rate irradiation.

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