STUDIES OF NA, MNA, NAD COMPOUNDS INFLUENCE ON RADIO-SUSCEPTIBILITY AND DNA REPAIR IN HUMANS LYMPHOCYTES

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Introduction: NA, MNA and NAD^+ compounds participate in many biological processes, including the regulation of energy metabolism, signal transduction and DNA repair. Nicotynamide (NA) is one of the two primary forms of vitamin B_3 (niacin). This compound is principal substrate in nicotinamide adenine dinucleotide (NAD^+) synthesis. Third investigated compound, methylnicotinamide (MNA) is metabolite of nicotynamide.

Objective: The aim of this study was to investigate the influence of the pre-treatment with NA, MNA and NAD^+ on the radiation induced DNA damage levels as well as on the DNA repair.

Methods: Thawed lymphocytes were incubated with fresh solutions of NA, MNA, NAD^+ in final concentrations 80 mM*. To evaluate influence of NA, MNA and NAD^+ on susceptibility to the induction of the DNA damage lymphocytes after the chemical pre-treatment were exposed to 2 Gy dose of X-rays and right after irradiation the extent of DNA damage was studied with the alkaline version of the single cell gel electrophoresis (SCGE) assay. To assess the influence of the pre-treatment with NA, MNA and NAD^+ on the DNA repair competency, the residual (unrepaired) DNA damage (RD) was detected with SCGE assay after 30 min. of incubation, in presence or absence of cellular mitogen PHA (phytohemagglutinin), long enough to complete the fast DNA repair process.

Results: Our results show statistically significant decrease in comparison to control of the DNA's radio-susceptibility in lymphocytes irradiated in presence of all investigated compounds. The percent of residual DNA damage in both proliferating and G0 cells, after pre-treatment with MNA or NAD^+ was similar or higher than controls. Presence of NA in G0 cells medium provide to decrease the residual DNA damage level (RDTM = 20.2 ± 12 for cells treated with NA and RDTM = 36.3 ±14 for control), however in proliferating cells presence of NA caused increase of the unrepaired DNA damage when compared with control (RDTM = 39.1±17 for cells treated with NA and RDTM = 15.8±13 for controls).

Conclusions: Our results suggested that all investigated compounds protected DNA during genotoxic agent action, but presence of these compounds during DNA repair processes disordered the efficiency of this process.

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