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DNA Oxidation in Patients with Metastastic Colorectal Cancer: Clinical Significance of 8-Hydroxy-Deoxyguanosine as an Independent Prognostic Factor

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Abstract

Introduction: Prognosis of metastatic colorectal cancer (mCRC) patients nowadays is an important subject in the field of oncology. R0-resection of colon with primary tumor and liver metastasis remains the only treatment which significantly improves survival rate. However, recent experimental data shows that surgical trauma can indirectly stimulate tumor growth due to mitochondrial dysfunction and unregulated superoxide radical (O2-.) generation.

Aim: To study the clinical significance of 8-hydroxy-deoxyguanosine (8-OHdGu) marker, to assess the oncological effects of heat ischemia of liver parenchyma on disease prognosis in patients with mCRC.

Material and methods: 69 urine 24-hour volume tests of patients with mCRC and 17 healthy individuals studied. Urine 8-OHdGu level measured using spectrophotometric method with pre-solid phase DNA extraction. The energy system and hepatocyte detoxification system state,levels of O2-. in tumor tissue determined using method of electron paramagnetic resonance (EPR) and SpinTraps technology at room temperature. Experiments carried out on a computerized EPR spectrometer RE-1307. EPR spectra recorded at temperature of liquid nitrogen (-196°C) in paramagnetically pure quartz dewar on a computerized spectrometer PE-1307 with resonator H011. Error of the method of spectrum integration and spread of spectrum reproduction of one sample is not more than 3%.

Results: The average level of marker in healthy individuals was 0.244 ± 0.063 nM/kg · day, whereas before the resection and on day 3 after the R0-resection of liver in mCRC patients -3.42 ± 0.18 nM/kg · day and 2,12 ± 0,08 nM/kg · days (p <0,05), respectively. On day 3 after the liver resection due to its metastatic lesions with a total duration of heat ischemia period<30 min and> 30 min have had marker at level 2,108 ± 0.13 nM/kg · day and 2.9883 ± 0.159 nM/kg · day (p <0.0001), respectively. The volume of metastatic tissue significantly and directly corelated with the level of urine 8-oxodGu (R2 = 0.54, 95% CI: 0.037-0.0991, p <0.000) ,also duration of surgical intervention(≥300 min) and duration of worm liver ischemia(>30 min.) during the surgery significantly increased urine level of 8-oxodGu (R2 = 0.54, 95% CI: 0.001 - 0.004, p <0.001).

Conclusions: Worm liver ischemia (>30 min.), long-term surgical intervention (≥300 min) and metastatic tissue volume (≥12 cm3) in liver parenchyma in mCRC patients significantly increase urine 8-OHdGu levels. R0-resection of liver metastases in mCRC patients dicreases urine 8-OHdGu levels already on day 3 after the surgery. 8-OHdGu is a new factor of oncological prognosis in patients with mCRC.

Key words: colorectal cancer, liver metastases, resection, warm ischemia injury, DNA damage