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Sex-related difference in the liver micronucleus assay using young rats

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Keywords: Liver micronucleus assay; Young rats; Sex-related difference

We assessed the sex-related difference in the liver micronucleus assay using young rats. Three and a half weeks old female and male F344 rats were orally treated with 50 mg/kg N-nitrosodimethylamine (DEN). Hepatocytes were isolated from anesthetized rats by the collagenase perfusion method on 3, 4 and 5 days after treatment and suspended in 10% buffered formalin. Then we observed hepatocytes under a fluorescent microscope (x400) after staining by AO (acridine orange) - DAPI (4',6-diamidino-2-phenylindole dihydrochloride) mixed solution. Micronucleus frequencies and mitotic index were assessed on analysis of 2000 hepatocytes.

The result showed that the micronucleus frequency of male increased with time-dependent manner and that of female kept almost constant during 3 days. However, there was no significant difference between them at the same sampling time. Moreover the micronucleus frequencies of both female and male treatment groups increased significantly compared with the control group on all sampling days, and the both judgements were clearly positive. From our result, we concluded that there was no sex-related difference in this assay for DEN.

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A possible mechanism for the enhancement by co-exposure to static magnetic fields of micronucleus formation by mutagens

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We have previously found that co-exposure to static magnetic fields (SMFs) increases the frequency of micronuclei induction by several mutagens. Recently, it has been reported that mutagenicity induced by active oxygen radical inducible chemicals increased after co-exposure to electromagnetic fields. Therefore, the increase in micronucleus formation by SMFs might be related to active oxygen radical inducibility. In the present study, we used the mouse bone marrow micronucleus test to investigate whether ascorbic acid can control the effects of SMF co-exposure on the frequency of micronuclei produced by radical-inducing chemicals. BALB/c mice were treated with ascorbic acid at a dose of 200 mg/kg body weight for 20 minutes before injection of doxorubicin (3 or 6 mg/kg) or mitomycin C (0.5 mg/kg). Mice were then immediately exposed to a 5-T SMF for 24 hours. After exposure to the SMF, bone marrow smears were stained with May-Grünwald-Giemsa. The number of micronucleated polychromatic erythrocytes in 1000 polychromatic erythrocytes was counted in each animal under a light microscope. Ascorbic acid itself did not induce micronuclei. The frequency of micronuclei induced by both doxorubicin and mitomycin C was increased by co-exposure to SMFs, but these increases were blocked by pretreatment with ascorbic acid. These results suggest that SMF exposure triggers the induction of mutagen-related radicals. This effect might increase the micronucleus frequency.