SHORT COMMUNICATION

Chemical Radiation Protection in Man as Revealed by Chromosome Aberrations in Peripheral Lymphocytes

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ABSTRACT

Patients with cervical carcinoma under radiotherapy have been followed during and after radiotherapy for the incidence of chromosome aberrations in peripheral lymphocytes. In patients treated with adrenochrome monoguanylydrazone methansulfonate (100 mg) before every irradiation the incidence was significantly lower than in those without the treatment. The result indicates chemical protection in man for the first time.

Chemical protection has a history of more than 20 years. Many chemicals such as cysteine, cysteamine, AET, and serotonin have been reported to protect animals against lethal doses of ionizing radiations but none of them have been demonstrated to protect human being. High toxicity of these chemicals has prevented their clinical application. Recently Sugahara and his colleagues reported that adrenochrome monoguanylydrazone methansulfonate (AMM) is radioprotective at very low doses in mice and suggested a promising future for its clinical application1,2. Yamashita et al. has tried to demonstrate its protective effect in man by using radiotherapy patients as materials3. Reduction in peripheral blood cell counts especially leucocyte count was much less in AMM-treated patients than in untreated controls. But because of a large physiological variation of these values it was very difficult to obtain statistically significant results. Many investigators did not agree with them to use leucocyte count as an indicator of radiation protection.
Recently chromosome aberrations in peripheral lymphocytes have attracted the attention of radiobiologists for their availability to biological dosimetry as reviewed in recent UNSCEAR report\(^4\). Correlation between the incidence of chromosome aberrations and radiation dose has been well established. In the present investigation chromosome aberrations in peripheral blood have been used as an indicator of radiation protection and chemical protection has been demonstrated in man by AMM. Patients with cervical carcinoma have been followed during and after radiotherapy. The lower abdominal region including the parametrium was irradiated with a pair of anterior-posterior and posterior-anterior fields of 14×14 cm each by a 6.0 MeV Liniac. Tumor dose was 150 rads per day, totalling 5,000 rads by repeating irradiations five times per week. Blood samples were taken from the patients 2 to 3 hours after about 1, 2, 3 and 5 krads and one week after the last exposure. Chromosome preparations were prepared according to a modification of the method of Moorhead et al.\(^5\). The culture time was 50 hours in all cases. Sixteen patients aged from 29 to 65 years were divided into two groups. One group was used as a control and the other group, protected, was administered with AMM in a dose of 100 mg intravenously within 20 min before every irradiation. Three hundred to 450 cells from 3 to 6 patients were scored in each group at every radiation dose mentioned above.

The increase in percent cells with acentric fragment and percent cells with dicentrics and rings in protected and control patients is shown in Figs. 1 and 2 respectively. Nonlinear increase in the incidence is quite in good accord with the results by Tamura et al.\(^6\). The increase in chromosome aberrations has been depressed in protected patients. By \(\chi^2\)-test the difference is statistically significant (\(p<0.05\)) at 3,000 R and 1 week after radiotherapy for acentrics and 1 week after radiotherapy for dicentrics and

![Fig. 1](image1.png)  
Fig. 1. Percent cells with acentric fragment in peripheral lymphocyte during and after radiotherapy. 150 rads per day, 5 times per week. × - × control patients, ○ --- ○ protected patients (AMM 100 mg intravenously within 20 min before irradiation).

![Fig. 2](image2.png)  
Fig. 2. Percent cells with dicentric and ring chromosomes in peripheral lymphocyte during and after radiotherapy. See for details the legend for Fig. 1.
rings. It must be noted that this depression is not apparent at 1,000 rads, i.e., ten days after the start of the radiotherapy.

By comparing the incidence with the in vitro data in the reference (UNSCEAR report 1969), the total blood dose has been estimated to be 145 rads in control patients and 110 rads in protected, dose reduction being about 30%. This protective effectiveness well corresponds to the dose reduction factor for LD 50/30 in mice, 1.32 as reported previously. However, there may be two arguments against this interpretation. First, if AMM protects lymphocytes in peripheral blood, the incidence of aberrations in protected cases should be below that in unprotected even at the first point of examination, i.e., after 1,000 rads. Second, since the patients irradiated only partially, the low incidence may result from the dilution of aberrant cells with normal cells from the non-irradiated region of the body. The dilution may be stimulated by AMM. But this is quite unlikely. Any way, the participation of cell kinetics in the pattern of chromosome aberrations in partial-body, fractionally irradiated patients as suggested by Tamura et al. cannot be discarded. If cell proliferation for supplementing lymphopenia induced by radiation starts after the second week of the radiotherapy, the cells in proliferation may better be protected by this chemicals than the cells in G0. A preliminary experiment by Kobayashi with Ehrlich ascites tumor cell in vivo suggests that AMM protects cells in S and G2 much better than cells in G1 by using the induction of chromosome aberrations by radiation as a criterion. Thus it may be concluded that the present result indicates for the first time the radiation protection by chemicals in man though its cellular mechanism remains to be elucidated. The authors are greatly indebted to Miss S. Oogami for her excellent technical assistance.

REFERENCES