THE DOSE RATE AS A MODIFIER OF BIOLOGICAL EFFECTS IN CONDITIONS OF THE COMBINED ACTION OF RADIATION-CHEMICAL FACTORS

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INTRODUCTION

The proper evaluation of the risk of the delayed effects in the case of equal absorbed doses but different dose rates in the conditions of the additional impact of the factors of nonradiation nature is a complicated biological and mathematical problem.

Insufficiently correct evaluation of the multi-factor effect of harmful substances on organizm and ascribing the registered negative aftereffects only to the impact of the radiation can result in both the overestimation of the radiation danger and the inefficient investments of funds into the system of countermeasures for reduction of risk of irradiation [1].

Taking into account the real character of the impact of the set factors of the radiation and nonradiation nature on organism, the effect of the dose rate has been studied in the conditions of additional influence of chemical compounds on the process of structural damages of chromosomes and induction of lung adenoma. Nitrogen oxides (one of the dominating atmospheric pollutants) and urethan, which is the pulmonotropic mutagen, have been chosen as chemical substances.

MATERIALS AND METHODS

The studies have been carried out using the mice of Af line in two series differ in the method of irradiation. In the first series mice have been exposed to the whole body single irradiation of Co gamma rays at a dose of 0.35 Gy and a dose rate of 1.0 Gy/h. In the second series the mice have been irradiated at a total dose of 0.35 Gy, but at a dose rate of 0.008 Gy/h (0.0389 Gy · 9 days).

Each series consisted of 8 groups: 1 - control, 2 - irradiation, 3 - inhalation of nitrogen oxides at a concentration of 120 mg/m^3 for 30 minutes, 4 - administration of urethane intraperitoneally (1 mg/g weight), 5 - inhalation of nitrogen oxides followed by administration of urethan an hour later, 6 - inhalation of nitrogen oxides in the same concentration an hour later after irradiation, 7 - administration of urethan an hour later after irradiation, 8 - the mice have been exposed to the action of three factors in the following sequence: irradiation + nitrogen oxides + urethan.

The cytogenetic analysis has been carried out on marrow cells in line with methods given in [2,3]. The cancerigenic effects have been determined according to the number of the induced lung adenoma in 20 weeks after the impact [4].

In groups of the combined effect of the factors, the coefficient of synergy (SC) has been determined with correction for the background [5].

RESULTS AND DISCUSSION

Chromosome aberrations (ChA)

The change of the frequency of the chromosome aberrations is shown on fig.2.

The spectrum of ChA has been presented by the fragments (single and pair), intrachromosome (cyclic rings) and interchromosome (symmetrical translocation) exchanges. The cells with multiple damages has also been registered.

The analysis of the spectrum has shown, that deletions have been the dominant type of aberrations in all experimental groups. The largest quantities of fragments have been found in the groups of the combined effect under a single exposure to radiation (up to 95% of all types of aberrations).

With prolongation of the dose, the fraction of simple deletions has been smaller and accounted for 75%. In the groups of the combined effect with lower dose rate, the aberrations of the chromosome type dominated. The number of the cyclic rings in case of the action of three factors against the background of the prolonged exposure to radiation has been four times as many as in the case of a single exposure to radiation under the same combination of factors (18.5% - 4.8% of the total number of ChA, respectively). In addition, the cells with multiple aberrations (more than 6) have been registered in this group.

The stable aberrations (total symmetrical exchange) have been under the three-factor effect with the background of prolonged exposure to radiation. The fraction of these aberrations in the total number of ChA has been 2.7% and 7.4% of the total number of ChA, respectively.

Lung adenoma

The induction of lung adenoma is shown on fig.2.

The effect of nitrogen oxides on mice under a single exposure to radiation was manifested as the inhibition of the process of adenoma formation in comparison with the separate effects. On the contrary, the prolongation of radiation exposure dose with inhalation oxides has been characterized by the increase of the frequency of adenoma - 2.06 (SC = 1.73).

In the group with combination of a single exposure to radiation and administration of urethan, the number of adenoma has reached the maximum value 14.06 adenoma/mouse, and SC = 4.46. The administration of urethan after the prolonged exposure to radiation has increased the cancerigenic effect, but the number of adenoma has been lower in comparison with the group of a single exposure to radiation, amounting to 4.31 (SC = 1.44).

In the group of three-factor effect and a single exposure to radiation, the number of adenoma/mouse has amounted to 6.67 (SC = 1.82). The prolonged exposure to radiation has increased these figures to 10.73 adenoma/mouse, and SC up to 3.48. With three-factor effect, SC in the group with the prolonged exposure to radiation has exceeded the indices of the similar group under a single exposure to radiation by a factor of two, and the growth of adenoma - by 1.6 times.

The treatment of the mechanisms of aberrations found out under the combined effect of radiation-chemical factors is significantly more complex as in the formation of ChA and tumor induction both the direct damage of DNA and the efficiency of functioning of the reparation system of a cell are important. The effect of the additional factors at this period can both strengthen the processes of restoration and facilitate its retardation especially in the cases, when the coefficient of synergy exceeds unity. The latter evidences the inclusion of additional mechanisms into the realization of registered changes, which are out of the scope of the additivity mechanisms.

The following mechanisms can be supposed as the above mentioned:

- Apart from the direct effect of each of the agents able to induce the DNA damage, possible additional influence on latent damages, which have been induced by the effect of the first agent, should be taken into account, including their transfer into the cytogenetically registered form, that is, ChA under the effect of the second agent [6, 7].
- Formation of a new substance from the active chemical compounds possessing mutagenic and cancerigenic properties intensifying the effects of precursors [8, 9].
- Stimulating effect of the ionizing radiation on the synthesis of carcinogenic agents [10].

It follows from the obtained data, that under the multi-factor effect, the reduction of the dose rate can result not in the increase, but in the decrease of frequencies of tumors. Therefore, the delayed consequences, associated with the dose effects, in particular, the processes of cancerigenesis, can be underevaluated in the real ecological conditions. Presently available observations on the alteration of the sensitivity of the irradiated organism to the effect of the nonradiation factors, as well as the radiation-chemical synthesis of mutagens from the containing in organism and the entering precursors confirm the possibility of existence of such a process [11, 12, 13].

Unsufficient evaluation of the modifying effect of radiation on the changes of the sensitivity of organism to the action of the chemical compounds, the level of which are considered to be safe, and attributing the registered modification only to the affect the scale and the direction of the countermeasures on elimination of the radiation risk.

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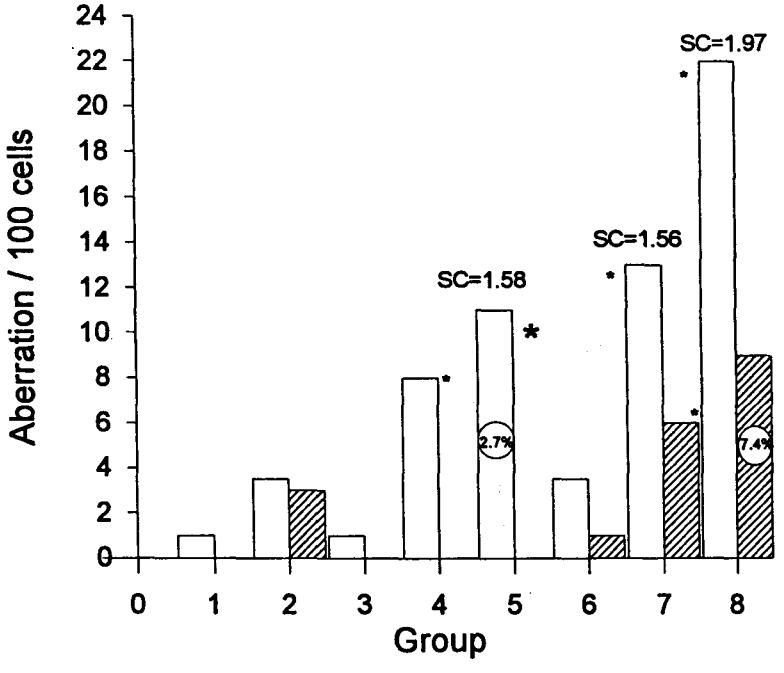

Fig.1. Frequency of chromosome aberrations in mice marrow cells
Y axis - number of aberrations on 100 metaphases
X axis - groups of experimental animals (in Materials and Methods)
- Total single γ-irradiation - prolongated γ - irradiation
- Presence of nonreparable aberrations
* - Difference is statistically reliable to control (P<0.05)

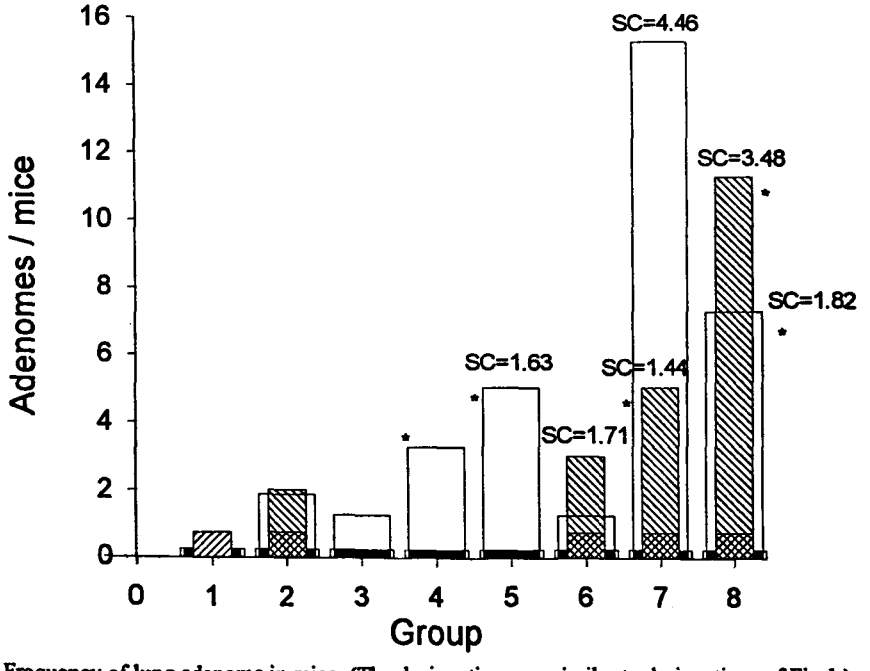

Fig.2. Frequency of lung adenoma in mice (The designations are similar to designations of Fig.1.)

- control of the group of total single γ- irradiation
- control of the group of prolongated γ - irradiation