PREVENTATIVE ANTICARCINOGENIC TREATMENT USING ANTIOXIDANT IMMUNOPROTECTIVE PREPARATIONS

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METHODS

On experimental model of external and internal exposure simulating various post-accidental situations, the effects of nitrogen-containing heterocyclic compounds with antioxidant and antiradical properties have been studied. The following irradiation schemes were used:

- Chronic gamma-exposure with dose rates of 0.25 and 0.50 Gy per week with accumulated dose 19 and 25 Gy.
- Continuous prolonged exposure with accumulated dose 10 Gy per month.
- Fractionated X-ray exposure 20 times per month, accumulated dose 10 Gy, with preliminary 2 days before single local 10 Gy exposure of the thyroid.
- Oral administration of 137 Cs (18.5 kBq/kg) every two months during 1.5 years. After 10 times administration for 600 days accumulated dose exceeded 21.0 Gy.

Survival rate, lethality dynamics, mean life span, cause of death and tumour induction rate have been registered as well as routine immunological, hematological and biochemical data.

RESULTS

The administration of the studied antioxidant compound as food additive increased the life span by 10-20 % in irradiated and non-irradiated animals showing the general positive gerontological effect (Fig.1a and 1b). At all levels of lethality of irradiated animals the mean life span was 2-2.5 months longer after the treatment in comparison with irradiated controls, and after exposure the effects of shortening of life span was diminished by 2 times. These data were statistically significant.

The mean life span is directly interrelated with lethality dynamics, and effect of antioxidant compound on this indicator has been confirmed, as for instance in the experiments with internal 137 Cs exposure (Fig.2). Lethality dynamics after 6 months of 137 Cs administration practically did not differ from intact controls. At the same time lethality of exposed animals without preparations significantly increased up to 24 %.
Life-span after chronic gamma-exposure of mice 0.25 Gy/week (A); rats after fractionated X-ray exposure (10.0 Gy accumulated) (B)

1. Irradiation
2. Control
3. Irradiation + compound 1 mg/kg
4. Compound
The lethality of treated animals at 240 days corresponded to that of nontreated group at 120 days (4 months advantage) and was two times lower than in the exposed controls at the same period.

The study of the compound effect on carcinogenesis first of all revealed 1.9 times lower incidence of spontaneous tumours in non-irradiated mice than in intact animals during 1.5 years of observation with some extension of life span (Fig. 3). After protracted gamma-exposure and compound administration a number of animals with tumours was 1.7-2 times lower than in irradiated but not treated rats.

Similar data have been obtained in cases with fractionated X-ray exposure. The effectiveness of the compound was mostly pronounced after 15-18 months, when lethality reached plateau. At this time tumorogenesis was inhibited by 2-2.5 times and corresponded to the levels in intact animals. The period of cancer mortality in treated animals was postponed up to 4-9 months (Fig. 3b), that indicated the maximal anticarcinogenic effect. In most experiments the highest effectiveness of antioxidants was observed after 1.5 years and later, when in irradiated control group a number of animals with tumours was at highest level. Fig. 4 presents data on a number of tumour carriers after 1.5 years in various chronic exposure models in comparison with irradiated non-treated and intact control groups taken as 100 % level. In all types of exposure with different doses of the administered antioxidant, significant anticarcinogenic effect has been observed, including the effect on spontaneous carcinogenesis (reduction of a number of tumours by 1.5-1.9 times) (Fig. 4).

The antioxidant also decreased the proportion of malignant tumours by 2-3 times and number of animals with multiple tumours (Fig. 4b). After sublethal exposure the antioxidant was highly effective in the improvement of general health indicators of the animal, such as weight increase, 30 % decrease of immunodepression, 1.5 times lower the leucopenia and some biochemical indicators.
Tumour induction in rats after protracted gamma-exposure (10 Gy accumulated) - A; fractionated X-ray-exposure (10 Gy accumulated) - B
0. Control 2. Irradiation+compound
1. Irradiation 3. Compound

Antioxidant compound effect on general number of tumours (A) and number of tumours (B) 1.5 years after exposure
1. Control 4.5. X-ray-exposure
2. Chronic gamma-exposure 6. Internal exposure
3. Protracted gamma-exposure
SUMMARY AND CONCLUSION

1. The tested compound is non-toxic and effective in relation to life span prolongation, mortality decrease etc., including general positive gerontological effects.
2. As radioprotector, the compound is effective before and after exposure administration and could be used for prevention and treatment.
3. Compound is effective as a general anticancerogenic agent for radiation-induced and spontaneous carcinogenesis.
4. The compound is non-toxic with the wide therapeutic spectrum in doses from 1.0-50.0 mg/kg of body weight and might be used as a food additive for a wide preventive distribution in population.

REFERENCES: