

Short-term exposure to high levels of natural external gamma radiation does not induce survival adaptive response

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Background: In some areas of Ramsar, a city in northern Iran, residents receive a much higher annual radiation exposure than is permitted for radiation workers. Induction of adaptive response in residents of Ramsar has been reported previously. In this study induction of such a response in short term exposure to high background levels of gamma radiation is investigated. **Materials and Methods:** Fifty male NMRI mice were randomly divided into four groups of 10-17 animals and 53 Wistar rats were randomly divided into five groups of 10-12 animals were studied. Animals in the 1st group were kept for 7 days in an outdoor area with normal background radiation while the 2nd, 3rd, 4th and 5th (in case of rats) groups were kept in 3 different outdoor areas with naturally elevated levels of gamma radiation. Animals were then exposed to a lethal dose of 8 Gy gamma radiation. **Results:** For mice, 30 days after exposure to lethal dose, the survival fraction for the control group was 40% while the 2nd, 3rd, and 4th groups had survival rates of 20%, 33.30%, and 35.20%, respectively. For rats, 30 days after exposure to the lethal dose, the survival fraction for the control group was 40% while the 2nd, 3rd, 4th and 5th groups had survival rates of 20%, 41.6%, 60.0% and 35.7%, respectively. **Conclusion:** Results indicate that short-term exposure to extremely high levels of natural gamma radiation (up to 196 times higher than the normal background) do not lead to induction of survival adaptive response. *Iran. J. Radiat. Res., 2012; 10(3-4): 165-170*

Keywords: Ramsar, natural background radiation, survival adaptive response, short term exposure.

INTRODUCTION

Ramsar a city in northern Iran is among the world's well-known inhabited areas with

highest levels of natural radiation. In areas with elevated levels of natural radiation annual exposure rates are up to 260 mSv y⁻¹ and average dose rates are about 10 mGy y⁻¹ for a population of about 2000 residents⁽¹⁻³⁾. Due to the local geology, which includes high levels of radium in rocks, soils, and groundwater, Ramsar residents are also exposed to high levels of alpha particles in the form of ingested radium and its decay progenies as well as very high radon levels in their dwellings (over 3000 Bq m⁻³ in some cases). It has been reported that the inhabitants of these areas receive doses much higher than the current ICRP-60 occupational dose limit of 20 mSv y⁻¹⁽⁴⁾.

Elevated levels of low dose rate natural radiation of Ramsar provide a unique opportunity to study epidemiological effects for the inhabitants. However to obtain reasonable and consistent data for 2000 residents, we need to observe them for long time to acquire considerable number of person-years for reliable statistical data. One of the low dose radiation effects is radioadaptation which has important implications for human health. Human and laboratory animal studies are indicative of occurrence of this phenomenon *in vivo*. The induction of the adaptive response in the

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lymphocytes of occupationally exposed hospital workers to X- and gamma rays⁽⁵⁻⁸⁾ and human lymphocytes exposed to the fallout from the Chernobyl accident⁽⁹⁾ are some sorts of these studies. *In vivo* experiments have also shown that low doses of radiation help protect against radiation-induced myeloid leukemia⁽¹⁰⁾ and spontaneous cancer in mice⁽¹¹⁾.

Radioadaptive responses of the residents who lived in high background radiation areas of Ramsar has been reported previously⁽¹⁾. Radioadaptation induced by natural background radiation has been shown to be more effective than occupational exposure⁽¹²⁾. It has also been shown that short-term exposure to elevated levels of radon could induce an adaptive response in laboratory animals⁽¹³⁾.

Recently Mortazavi *et al.* have shown that short-term exposure to artificially elevated levels of radon may induce an adaptive response in an animal model⁽¹³⁾. In this study we investigate the possible induction of oxidative stress after short-term exposure to extremely high levels of natural radiation. In addition, since there is no report on the induction of adaptive response in short term exposures to high background levels of gamma radiation, the main aim of this study is to verify if exposure of laboratory animals to extremely elevated levels of natural external gamma in high background radiation areas of Ramsar can lead to induction of survival adaptive response.

MATERIALS AND METHODS

Animals

Fifty male NMRI mice (age 3 weeks, 25-30 g) and 53 male Wistar rats (age 9 weeks, 200-250 g) were purchased from Pasteur and Razi Institute in Amol, Iran, respectively. Mice were randomly divided into four groups of 10-17 animals and rats were randomly divided into five groups of 10-12 animals. Animals were kept under a 12-hour light and 12-hour dark cycle at

ambient temperature (21 ± 1 °C) with free access to food and water. All guidelines of Shiraz University of Medical Sciences (SUMS) for ethical treatment of animals were observed.

Exposure to naturally elevated levels of radiation

In the first phase of this study, animals in the 1st group were kept for 7 days in an outdoor area with normal background radiation (0.10 μ Sv/h) while the 2nd, 3rd, and 4th groups were kept for 7 days in Talesh Mahalleh, Ramsar with 3 different naturally elevated levels of gamma radiation of 0.64, 2.09 and 3.73 μ Sv/h, respectively. A calibrated RDS-110 survey meter (RADOS Technology, Finland), mounted on a tripod approximately 1 meter above the ground, was used to measure exposure rate at each location. In the second phase of the study, higher dose rates of natural radiation were investigated (in the 1st phase the highest dose rate was only 37 times greater than the normal background). Therefore, animals in the 1st group were kept for 7 days in an outdoor area with normal background radiation (0.18 μ Sv/h) while the 2nd, 3rd, 4th and 5th groups were kept in 4 different outdoor areas with naturally elevated levels of gamma radiation in Ramsar; i.e. 3.92, 8.47, 16.43 and 35.28 μ Sv/h, respectively. Thus we were able to examine the effects of dose rates as high as 196 times the background level.

Exposure to lethal dose

On day 8, all animals were exposed to 8 Gy gamma radiations emitted by a Theratron Phoenix (Theratronics, Canada) Cobalt-60 therapeutic source (dose rate 55 cGy/min) at Radiotherapy Department of Razi Hospital in Rasht, Iran.

Survival study

After irradiation rats were moved back to their cages and their survival was carefully monitored three times a day for 30 days. Kaplan-Meier survival analysis (SPSS 17.0)

was used to evaluate the statistical significance of the differences of survival rates among different groups.

RESULTS

As shown in table 1, in the first phase of the study with NMRI mice, survival rate in the control group (only exposed to lethal dose) was 90% on day 24, while the survival rates for those animals pre-irradiated with low, moderate and high dose rates of natural radiation before exposure to lethal dose were 40%, 75% and 64.7%, respectively. Thirty days after exposure to lethal dose of gamma radiation, the survival fraction for the control group was 40% while the 2nd, 3rd, and 4th groups had survival rates of 20%, 33.30%, and 35.20%, respectively.

As shown in table 2, in the second phase of the study with rats, survival rate in the control group (those exposed to normal background radiation of 0.18 $\mu\text{Sv/h}$) was 40% on day 25, while the survival rates for those animals exposed to higher levels of

natural radiation before irradiation with lethal dose; i.e. 3.92, 8.47, 16.43 and 35.28 $\mu\text{Sv/h}$, were 20%, 41.6% and 60% and 35.7%, respectively. Kaplan-Meier survival analysis could not reveal any statistical significance differences in survival rates among different groups for the 1st phase of the study ($P=0.717$) and the 2nd phase ($P=0.362$). Pair-wise comparisons also could not show any significance differences in survival rates between each two groups (i.e. survival rate of the animals kept in an area with a dose rate of 0.18 $\mu\text{Sv/hr}$ as compared to that of 3.93, 8.48, 16.43 or 35.28 $\mu\text{Sv/hr}$). Figures 1 and 2 show the survival rates of the animals in 30 days for the 1st phase and in 25 days for the 2nd phase of the study, respectively.

DISCUSSION

In our previous cytogenetic studies, after *in vitro* irradiation with a challenge dose of gamma rays, a significant cytogenetic adaptive response was observed in the

Table 1. The pattern of exposure to high levels of natural radiation in different groups.

Group	Dose Rate ($\mu\text{Sv h}^{-1}$)	Survival Rate 30 Days After Exposure to lethal Dose
G1 (Normal Background)	0.10	40%
G2 (HBRA-1)	0.64	20%
G3 (HBRA-1)	2.09	33.3%
G4 (HBRA-1)	3.73	35.2%

G- Group
HBRA – High Background Radiation Area

Table 2. The pattern of exposure to high levels of natural radiation in different groups.

Group	Dose Rate ($\mu\text{Sv h}^{-1}$)	Survival Rate 30 Days after Exposure to Lethal Dose
G1 (Normal Background)	0.18 $\mu\text{Sv/hr}$	40%
G2 (HBRA-1)	3.93 $\mu\text{Sv/hr}$	20%
G3 (HBRA-2)	8.48 $\mu\text{Sv/hr}$	41.6%
G4 (HBRA-3)	16.43 $\mu\text{Sv/hr}$	60%
G5 (HBRA-4)	35.28 $\mu\text{Sv/hr}$	35.7%

G- Group
HBRA – High Background Radiation Area

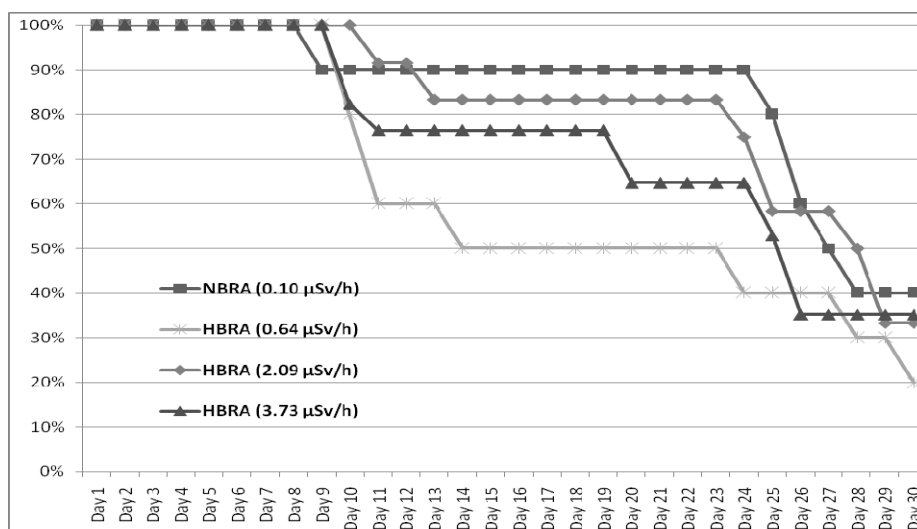


Figure 1. Survival plots of different groups within 30 days after irradiation of mice pretreated with various low doses of NHLR for 7 days.

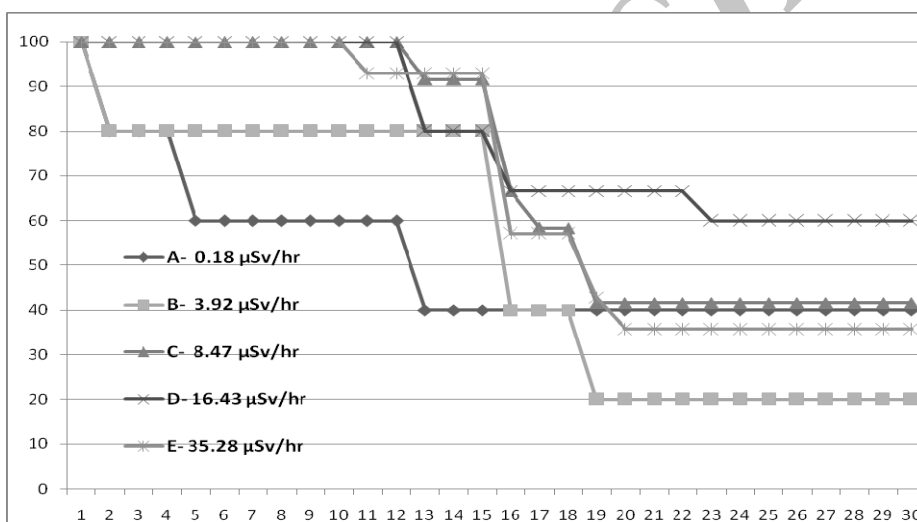


Figure 2. Survival plots of different groups within 30 days after irradiation of mice pretreated with various low doses of NHLR for 7 days.

lymphocytes of residents of the very high background radiation areas of Ramsar ⁽¹⁾. However, in spite of methodological differences, results obtained in both phases of this study show that high levels of natural radiation cannot induce survival adaptive response. Moreover, current findings are not consistent with the results obtained in our previous study on the induction of adaptive response in laboratory animals after short-term exposure to elevated levels of radon ⁽¹³⁾. The discrepancies in these findings might reside on cellular response to low levels of ionizing radiation. Similar to all biological

responses of cells to IR induced or exogenous stress ⁽¹⁴⁾, inducible cellular processes occurring in cells following exposure to low doses of ionizing radiation is mediated through DNA damage. These evidences show that radiation has a stimulating effect on a number of biological processes and can induce resistance against higher doses of ionizing radiation.

In early studies, Feinendegen *et al.* proposed that adaptive response could be induced by reactive oxygen species (ROS) ^(15, 16). The ROS refers to a group of molecules including peroxides and free radicals which

are derived from oxygen and are highly reactive toward biomolecules⁽¹⁷⁾. ROS react with critical biomolecules such as DNA and induce oxidative stress (imbalance of prooxidants versus antioxidants) and damage in these macromolecules, multiple localized lesions such as base damage, single strand breaks (SSBs) and double strand breaks (DSBs), DNA-DNA cross links and DNA-protein cross links⁽¹⁸⁻²¹⁾. As indicated by some investigators⁽²²⁻²⁴⁾, we believe that induction of adaptive response by pre-exposure to ionizing radiation needs a minimum level of damage that triggers this phenomenon and increases the resistance of living organisms (*in vivo*) or cells (*in vitro*) to higher levels of the same or of other sources of stress.

Findings of this study show that in contrary with the results obtained in short term exposure to radon, exposure of animals to naturally elevated levels of gamma radiation does not lead to the induction of survival adaptive response. Consistent with our previously reported data^(2, 25-34), radiobiological studies on the health effects of the chronic exposure to elevated levels of natural radiation in residents of areas such as Ramsar may lead to the identification of the cellular and molecular mechanisms by which susceptibility to genetic damage and cancer is decreased by chronic radiation exposure. These findings might have implications in areas such as radiation therapy, radiation protection and even selection of appropriate candidates for long term manned space missions⁽³⁵⁾.

Conflict of interest:

None Declared

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