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BODY WEIGHT KINETICS OF F_1 GENERATION IRRADIATED *In-utero*

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AUTHORS' CONTRIBUTIONS

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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ABSTRACT

To investigate radiation risks associated with a low dose and low dose rates, pregnant Swiss albino mice were exposed to 0.20 Gy, 0.40Gy and 0.80 Gy of gamma rays from a Cobalt-60 source at two different dose rates (0.0584 Gy/min and 0.00091 Gy/min) on 18-day post conception. Irradiated as well as control animals were allowed to reach term and to deliver normally. Post irradiation variations in the body weight of mice were studied in the F1 generation at 0 days and 1,2,3,4,5,6 and 12 weeks of postpartum age. Bodyweight at both and at different postnatal ages was found to be influenced by the exposure dose as well as by the dose rate. The higher the dose, the greater is the weight loss. Moreover, at different postnatal age's body weight was less in the High dose rate (HDR) subgroup than in the Low dose rate (LDR) subgroup. This holds true for all the exposed dose groups. In all the dose groups ratio of LDR to HDR, values for the bodyweight revealed the following relation: 0.20 Gy < 0.40Gy < 0.80 Gy.

Keywords: Postpartum; dose-rate; gamma radiation; Swiss albino mice.

1. INTRODUCTION

Life forms and processes are more susceptible to toxic action when they are in developmental stages than when they have reached maturity. In comparison to adults, ionizing radiation is more disastrous to unborn babies. High doses of radiation are incredibly pernicious to tissues and cells. However, the biological effects of low dose or low dose rates of ionizing radiation remain unclear. Recently there has been increased interest in the biological effects of low dose or low dose-rate of ionizing radiation on normal tissues [1,2]. These effects probably include cell proliferation, cell cycle disturbance, cell death [3,4], circulation and metabolism [5] and other related effects on the immune system [6].

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The fetal body weight is a sensitive and precise indicator for growth retardation effects of intrauterine radiation exposure [7]. Post irradiation body-weight studies have been done by a large number of scientists, but the dose-rate effect on the body weight of mice is still not apparent. Therefore, the primary concern of the present investigation is to assess the impact of low doses of Gamma radiation delivered at different dose rates on the unborn mice and its bearing through postnatal development.

2. MATERIALS AND METHODS

2.1 Animal Care & Handling

The animal care and handling were performed according to the guidelines set by WHO (World Health Organization) and INSA (Indian National Science Academy, New Delhi). Swiss albino mice (*Mus musculus*) were used in the present study and were initially procured from Central Drug Research Institute (CDRI), Lucknow, India. They were housed in a well-ventilated room with optimum light and temperature, fed on standard mice feed acquired from Lipton India Ltd., New Delhi, and tap water supplied *ad libitum.* Occasionally sprouted grams were served along with the feed. Tetracycline water was given sometimes to prevent infection. A close-bred colony of 100 mice was maintained by random brother and sister mating of animals, with a ratio of 3 females- :1 male per cage (75 females and 25 males). Out of the 75 females all got pregnant and were studied in sequence of their pregnancies.

2.2 Sources of Irradiation

The animals were irradiated by means of a Co-60 radiography camera with a pencil source procured from Bhabha Atomic Research Center, Trombay. Exposure operations were carried out from a safe distance of 10 meters with the help of a gear-box assembly. No anesthesia was given, only physical restraint was used.

2.3 Experimental Design

Pregnant females of 18 days- post-conception (d.p.c.) were selected and irradiated with a total dose of 0.20 Gy, 0.40 Gy, and 0.80 Gy of Gamma rays. Each dose is delivered at 2 different dose-rates:

a. Low dose rate (LDR) 0.00091 Gy/min
b. High dose rate (HDR) 0.0584 Gy/min

2.4 Parameters

Sham exposed females were maintained for all the experimental groups. This group served as the control. Irradiated as well as control animals were allowed to reach term and to deliver normally. Pregnancy of mice was confirmed by the vaginal plug method. From each group, 5 animals were autopsied at 1 day, 3 days and 1,2,4,6 and 12 weeks of postpartum ages. The pups were weighed on the day of parturition and then their weight was recorded weekly up to 12 weeks of age. Separate records were maintained for male and female pups. The body weights taken were converted into a percentage, considering the control weight as 100 percent.

2.5 Statistics

All the data were analyzed by the Student's t-test. The significance level was obtained from the table of significance provided for the Student's t-distribution. The significance level of 0.5, 0.05, and 0.001 was used.

3. RESULTS AND DISCUSSION

Experimental studies revealed that all irradiated females' progeny exhibited weight loss at different postnatal ages. This is in agreement with the observations made by Dev *et al,* [8]. They also observed that exposure of mice during the fetal period resulted in significant weight loss during postnatal life. A reduction in body weight of offspring at different postpartum ages after *in utero* exposure had also been recorded by Bhatia and Sisodia [9] and Mathur [10]. Body-weight at birth and at different postnatal ages was found to be influenced by the exposure dose as well as by the dose-rate. Yi et al., [11] also described that the frequency and severity of radio lesions vary as a result of the difference in amount and dose-rates. In the present work also, a more significant weight loss was observed in the progeny of the females who were exposed to a total dose of 0.80 Gy than in those which were born to females irradiated with the total dose of 0.40 Gy or 0.20 Gy.

From the body-weight tables 1 and 2 it is evident that radiation induces a loss in body weight, but the pattern of weight loss of male progeny resembles those of female progeny only at early intervals: at later intervals, the pattern becomes different. The male and female neonates born in all the experimental groups exhibited a weight loss at birth which continued till one week of age. This represents the first phase of growth retardation. The first phase of growth retardation was followed by a recovery during which a steady weight gain was noticeable. The graphical representation is shown in Figs. 1 and 2- for this text.

However, after a partial recovery of the body weight, male progeny exhibited the second phase of growth

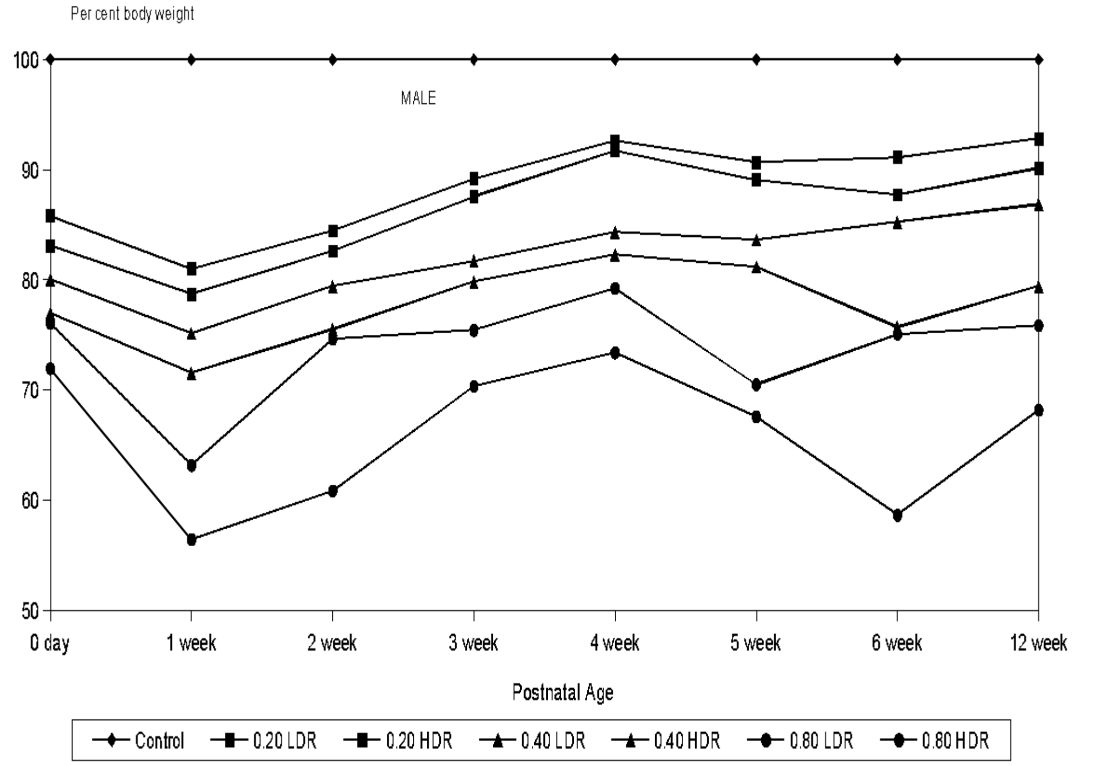

Fig. 1. Percent body weight of male mice exposed at d.p.c to different doses and dose-rates of gamma rays

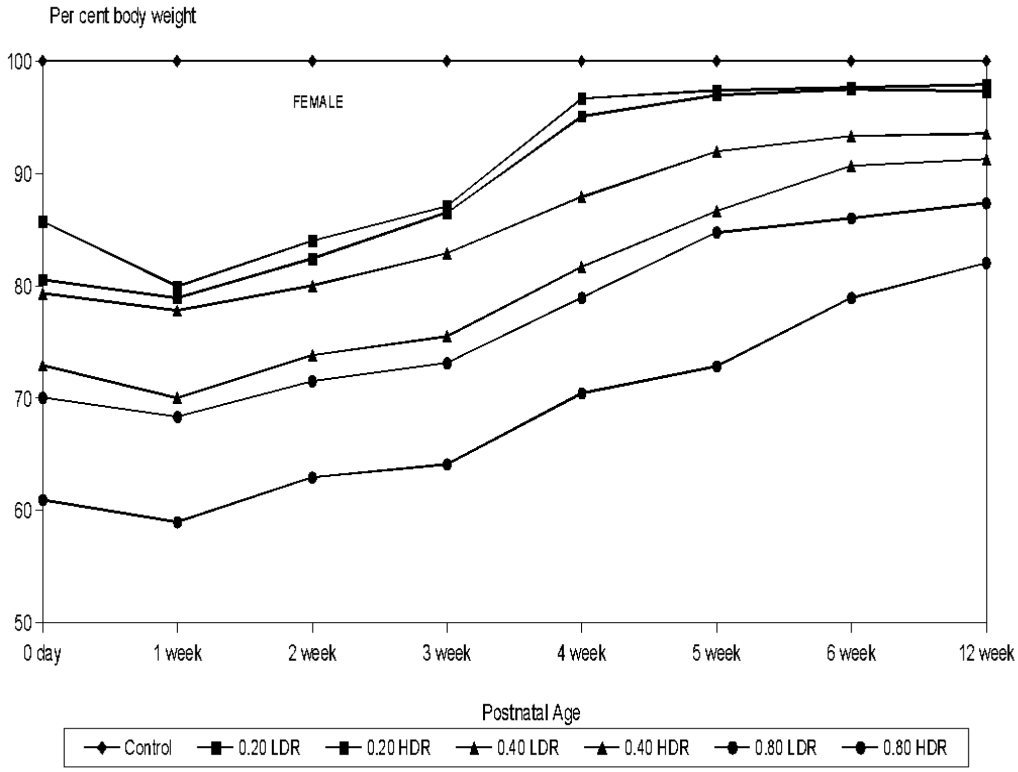

Fig. 2. Percent body weight of female mice exposed at 18 d.p.c to different doses and dose-rates of gamma rays

Table 1. Influence of prenatal exposure at 18 d.p.c to different doses and dose-rates on percent body weight of male mice

Exposure		Postnatal age (in weeks)							
Dose (in Gy)	**Dose-rate (in Gy/min)**	**0 Day**	**1**	**2**	**3**	**4**	**5**	**6**	**12**
Control		2.10 ±0.73	4.77 ±0.50	5.80 ±0.91	6.90 ±0.64	14.76 ±0.87	17.26 ±1.04	12.31 ±0.76	21.65 ±1.01
0.20	0.00091	85.80 ±0.20	80.99 ±0.12	84.42 ±0.10	89.17 ±0.87	92.60 ±1.04	90.64 ±0.71	91.10 ±1.03	92.80 ±0.96
	0.0584	83.08 ±0.19	78.67 ±0.18	82.59 ±0.26	87.55 ±1.10	91.88 ±1.00	89.08 ±0.87	87.69 ±1.07	90.12 ±0.56
0.40	0.00091	80.00 ±0.12	75.13 ±0.69	79.14 ±0.10	81.69 ±1.00	84.30 ±0.92	83.62 ±2.0	85.21 ±1.07	86.83 ±1.15
	0.0584	76.92 ±0.41	71.52 ±0.73	75.48 ±0.12	79.81 ±1.01	82.26 ±1.31	81.17 ±1.9	75.69 ±1.7	79.40 ±0.85
0.80	0.00091	76.05 ±0.32	63.12 ±0.26	74.61 ±0.3	75.39 ±0.91	79.20 ±0.98	70.47 ±1.03	75.06 ±1.08	75.84 ±1.24
	0.0584	71.92 ±0.21	56.40 ±0.23	60.81 ±0.29	70.31 ±0.86	73.36 ±1.01	67.54 ±1.12	58.61 ±1.32	68.16 ±1.43

** control weight is in grams*

Table 2. Influence of prenatal exposure at 18 d.p.c to different doses and dose-rates on percent body weight of female mice

Exposure		Postnatal age (in weeks)							
Dose (in Gy)	**Dose-rate (in Gy/min)**	**0 Day**	**1**	**2**	**3**	**4**	**5**	**6**	**12**
Control		2.10 ±0.73	4.60 ±0.96	5.80 ±0.51	6.79 ±0.64	13.34 ±0.91	16.18 ±0.72	17.50 ±0.47	19.38 ±1.02
0.20	0.00091	85.70 ±0.12	79.93 ±0.6	84.00 ±0.91	87.10 ±1.01	96.66 ±1.52	97.39 ±1.03	97.66 ±1.01	97.90 ±1.03
	0.0584	80.52 ±0.21	78.90 ±0.51	82.40 ±0.70	86.51 ±0.81	95.09 ±0.92	96.99 ±1.10	97.50 ±1.00	97.30 ±1.01
0.40	0.00091	79.31 ±0.32	77.78 ±0.12	80.00 ±0.3	82.90 ±0.62	87.91 ±1.21	91.95 ±1.53	93.52 ±1.50	93.55 ±0.93
	0.0584	72.90 ±0.21	70.00 ±0.11	73.81 ±0.53	75.48 ±0.83	81.68 ±0.97	86.63 ±0.72	90.66 ±1.01	91.30 ±1.05
0.80	0.00091	70.01 ±0.12	68.31 ±0.14	71.48 ±0.56	73.10 ±0.64	78.91 ±0.89	84.74 ±1.01	86.01 ±0.89	87.36 ±0.89
	0.0584	60.90 ±0.10	58.92 ±0.09	62.89 ±0.91	64.08 ±0.79	70.41 ±1.21	72.81 ±1.03	78.91 ±1.07	82.03 ±0.83

** control weight is in grams*

Table 3. LDR/HDR of the body weight of the male mice at different postnatal ages after prenatal exposure at 18 d.p.c to different doses

Dose	Postnatal Age (in weeks)							
(in Gy)	**0 Day**	**1**	**2**	**3**	**4**	**5**	**6**	**12**
0.20	1.03	1.03	1.02	1.01	1.00	1.01	1.04	1.03
0.40	1.04	1.05	1.04	1.02	1.02	1.03	1.12	1.09
0.80	1.05	1.11	1.22	1.07	1.08	1.04	1.28	1.11

retardation when the body- weight fell again. This second phase was not evident in the female progeny. When the percent body weights were plotted against the postnatal ages of the offspring, a clear biphasic mode of weight loss in male offspring and a monophasic mode in female offspring were observed. The biphasic mode of weight loss was more evident in HDR subgroups than LDR subgroups. They were suggesting that the same dose delivered at a lower dose rate minimized the second phase of growth retardation. Due to biphasic mode the weight loss curve of male progeny appeared "W" shaped. A biphasic mode of weight production ("W" shaped curve) was initially proposed by Dev et. *al.,* [12] where the second phase could be averted either by reducing the total dose or by the introduction of a radio-protective drug. Unlike male progeny, the female progeny continued to grow after the first phase of weight loss. Their weight loss curve is "V" shaped, suggesting that in female progeny a second fall in the growth had been averted.

Radiation- induced cell death was probably responsible for a decrease in body weight [13], Wilson et al., [14], Aziz et al., [15], Srivastava et al., [16]. The first phase of weight loss in both male and female offspring could be attributed to radiation-induced growth retardation due to cell loss. Dev et. *al.,* [8] also noted that the female neonates are less vulnerable than the male neonates after irradiation with 0.50 Gy gamma rays. Postnatal reduction in the body weight directly expressed the radiation induced growth retardation of fetuses [7]. The second phase of weight loss observed in the males of all the dose groups could be due to the absence of progesterone which is available in females helping in fat deposition, thereby preventing the second phase of weight loss.

In order to find out the difference in the degree of radiation effects caused by the LDR and HDR of the same total dose, taking body weight as an end parameter, the ratio of LDR to HDR values (LDR/HDR) was calculated for each post-irradiation interval for the 3 doses i.e., 0.20 Gy, 0.40 Gy, and 0.80 Gy as shown in Table 3. It was found to be minimum for 0.20 Gy and maximum for the 0.80 Gy group.

4. CONCLUSION

The following main conclusions may be drawn from the above findings:

- The effect of radiation was found to be dose-dependent. Maximum radio lesions were observed in 0.80 Gy group and minimum in 0.20 Gy group.
- Prenatal exposure of pregnant females on 18 d.p.c. induced a reduction in body weight. Male progeny exhibited a biphasic mode of weight loss, while a monophasic mode of weight loss was manifested by female progeny.
- The ratio of LDR to HDR values for the body-weight revealed the following relation: 0.20 Gy < 0.40 Gy < 0.80 Gy.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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