[***Radiobiol. Radiother.*** (1985): (26), H.3, 385]

Liv.52 Protection Against Radiation-Induced Abnormalities on Mammalian Prenatal Development

Saini, M.R., Kumar, S. and **Saini, N.**
The Radiation Biology Laboratory, Department of Zoology, University of Rajasthan, Jaipur
and Department of Paediatrics, E.S.I. Hospital, Jaipur, India

INTRODUCTION

Developing mammalian embryo is more sensitive to ionizing radiation than adults. Many experimental studies have shown that radiation-induced abnormalities in mammals are closely related to the period of development at which radiation is given[1,2]. Many SH-compounds like cysteamine, AET, MEG and WR-2721 have been reported to protect animals against radiation injuries, but their clinical applications have been found to be very much limited because of high toxicity[3-6]. Very recently authors have observed the radioprotective effect of an indigenous drug commercially known as Liv.52, which is being used as a detoxicating agent with a wide range of applications in various hepatic disorders[7-13]. Therefore, the present study deals with the protective role of Liv.52 in modifying the radiation-induced malformations in embryos.

MATERIALS AND METHODS

Pregnant Swiss albino mice at 11 day gestation period were selected from an inbred colony maintained on standard mice feed (procured from Hindustan Lever Ltd., New Delhi) and water *ad libitum* (indication of vaginal plugs was considered zero day of pregnancy). Females were divided into two groups of 10 each, experimental (Liv.52 treated) and control (non-drug treated). The experimental animals received a daily oral dose of 0.05 ml/animal of Liv.52 (received from The Himalaya Drug Co., Bombay, India, in the form of drops) for 11 days prior and post-irradiation, while animals of the control group were administered an equal volume of tap water in a similar manner. After 11 days of this treatment the animals of both the groups were exposed to 2.5 Gy gamma radiation, in a well-ventilated plastic box at the dose rate of 0.8 Gy/min.

All the females were observed till term and after parturition, their offspring were studied from birth to 10 months of age with regard to litter size, sex ratio, mortality and abnormalities. For the skeletal abnormalities skiagrams were made of the animals after 10 months of age.

RESULTS

The control females showed complete resorption of embryos after exposure while there was no resorption of embryos, reduction in litter size and alteration in sex ratio of newborns in experimental animals. However, 25% mortality was recorded within 15 days in the newborns of experimental animals and 80 per cent of the remaining animals showed fused vertebrae in the caudal region, while the remaining mice were normal in all respects.

DISCUSSION

It is an established fact that developmental malformations initiated by prenatal X or gamma irradiations are determined by several factors: stage of development and type of radiation. Russell and Nash and Gowen[2] reported that the period of organogenesis is more radiosensitive than the fetal growth period as far as resorption, litter size and mortality of young ones are concerned, and the

gestation day 11½ is close to the stage of maximum susceptibility for growth retardation[1]. It is also reported that significant killing action of 200 R resulted in at least 88.1 percent reduction in average litter size at birth[14]. They also showed a 100 per cent death of embryos with 400 R within 24 hours of exposure. Dev *et al.*[15], observed the complete resorption of embryos of both protected and unprotected females at 11¼ day gestation after exposure with 250 R. Similarly in the present study, we have also observed 100 per cent resorption of embryos in the control group. It appears that resorption is directly related to the intrauterine killing of embryos.

Hicks and D'Amato[16] advocated that selective mitotic cell death (at G-2 phase of cell cycle) of certain classes of primitive cells at various sites is the principal effect of ionizing radiation in the embryos. It also changes proliferation rate (at least transiently) and alters differentiation of individual cells and cell population, sometimes in ways that are bizarre and possibly unique. Depending on the regulative capacity of the surviving cells, i.e. their ability to take over the duties of the lost cells and catch up with unaffected parts, there may be excellent restitution with the appearance of normal development or malformation may result. Ershoff *et al.*[17], have shown that AET, cysteamine and MEG largely prevented the occurrence of foot deformation when exposed to a single dose of 150 R whole-body gamma radiation. However, in the present experiment, females treated with Liv.52 before irradiation showed 100 per cent parturition, but 25 per cent mortality was recorded within 15 days in the newborns and the remaining 80 per cent young ones showed no malformation except fusion of vertebrae in the caudal region. Liv.52 also protected the prenatally irradiated animals from radiation-induced reduction in post-natal growth and weight. This is in agreement with the findings of the other workers.

It appears that Liv.52 may increase the spontaneous food consumption and food conversion in the pregnant by protecting the liver, which plays an important role in the general metabolism, pass into the fetus through the placental barrier and neutralize the peroxides formed from water molecules after irradiation.

SUMMARY

Pregnant Swiss albino mice were whole body exposed to 2.5 Gy gamma rays with or without Liv.52 during the selective organogenesis period. The control pregnant mice of 11 day gestation showed complete resorption of embryos while the drug-treated females showed normal parturition. There was no reduction in litter size and alteration of sex ratio of the newborns. However 25 per cent mortality was recorded within 15 days in the newborns. In most of the remaining animals fusion of the vertebrae was observed in the caudal region.

Key words: Liv.52 irradiation, fused vertebrae, SH-compounds.

REFERENCES

1. Russell, L.B., "The effect of radiation on mammalian prenatal development" in Radiation Biology, Vol. I, Part II, pp. 861. (McGraw Hill, New York, 1954).

2. Nash, D.J. and Gowen, J.W., "Effects of X-irradiation upon postnatal growth in mouse:, *Biol. Bull*. (1962): 122, 115.

3. Maisin, H., Dunjie, H., Maldague, P. and Maisin, J., "Au suget de la protection des embryos irradies in iutero par la mercaptoethlamine", *C.R. Sean, Soc. Biol.* (1955): 149, 1687.

4. Rugh, R. and Clugston, H., "Protection of mouse fetus against X-irradiation death", *Science* (1956): 123, 28.

5. Robert, J.M. "Cysteamine protection against lethal and growth inhibiting effect of prenatal X and gamma irradiation", *Teratology* (1970): 3, 319.

6. Nagata, H., "Studies on sulfhydryl radio-protector with low toxicity", *Tokushima J. Exper. Med*. (1980): 27, 15.

7. Mathur, P.S., "Some chemical observations on the use of Liv.52 (an indienous drug) in cases of cirrhosis of the liver in children", *Curr. Med. Pract*. (1957): 1, 107.

8. Joglekar, G.V., Chitale, G.K. and Balwani, J.H., "Protection by indigenous drug against hepatotoxic effects of carbon tetrachloride in mice", *Acta pharmacol et toxicol.* (1963): 20, 73.

9. Karandikar, S.M., Joglekar, G.V., Chitale, G.K. and Balwani, J.H. "Protection by indigenous drug against hepatotoxic effects of carbon tetrachloride – long term study", *Acta pharmacol et toxicol*. (1963): 20, 274.

10. Sule, C.R., Pai, V.R., Damania, R.F., and Joshi, V.S., "Studies with Liv.52 therapy in infective hepatitis", *J. Ind. Med. Prof.* (1968): 14, 6391.

11. Arora, J.K., "Role of various types of treatment in infectious hepatitis", *Arm. Forc. Med. J*. (1969): 25, 362.

12. Deshpande, R.S., Sheth, S.C. and Joykutty, N.D., "Infectious hepatitis – Study of 100 cases", *Curr. Med. Pract*. (1971): 15, 810.

13. Patel, G.T., Mruthyunjayanna, B.P., Seetharam, T.D. and Gowda, A.C.C., "Liv.52 therapy in viral hepatitis", *Probe* (1972): 11, 112

14. Wilson J.G. and Karr J.W., "Effect of irradiation on the embryonic development. L. X-ray on the 10^{th} day of gestation in the rat", *Amer. J. Anat*. (1951): 88, 1

15. Dev, P.K., Pareek, B.P., Goyal, P. K., Mehta, G. and Gupta, S.M., "Effects of prenatal gamma radiation on the development of mice and its modification by MPG," *Acta Anat*. (in press).

16. Hicks, S.P. and Amato, C. J'D, "Effect of ionizing radiation on mammalian development"; in Advances in teratology; Vol. 1, pp. 195-259 (Longos Press Limited, London 1966).

17. Ershoff, B.H., Steers, C.W. and Kruger, Jr. L., "Effect of radio-protective agent on foot deformities and gain defect in the prenatally X-irradiated rat", *Proc. Soc. Exp. Biol. and Med*. (1962): III, 391.