RESPONSES OF GAMMA IRRADIATED MICE TO α-TOCOPHEROL

N. M. Eliosoff, D. Dubner and P. Gisone

Comisión Nacional de Energía Atómica
Gerencia de Seguridad Radiológica y Nuclear
Buenos Aires. Argentina

ABSTRACT

CB57 female mice whole body gamma irradiated were orally administered with acetato DL-α-tocopherol. It was observed a higher survival in α-tocopherol treated groups up to 14 th and 10th days with doses of 8.5 and 10 Gy respectively and a greater bone marrow cellularity at day 10 in α-tocopherol treated group irradiated with 10 Gy.

INTRODUCTION

Radiation-induced damage to biological membranes is important because these celular elements perform a decisive role in the functional organization of the cell. In view of the importance of α-tocopherol in membrane structure, we chose this drug to test its action not only in protecting against initial radiation damage but also in the recovery from radiation stress.

Rejholcovà and als. (1) found an increase in lipid peroxidation from the 13th pòstirradiation day after doses of 6.8 Gy. They suggested this peroxidation was the result of metabolic disorganization caused by the radiation sickness.

In this work we used higher doses of radiation (8.5 and 10 Gy) and assuming that increase in lipid peroxidation could be observed earlier, the α-tocopherol was administered to mice inmediately after exposure and 4 and 7 days later.

MATERIAL AND METHODS

CB57 female mice, 8 weeks old, weighing 18-20g were whole body gamma irradiated with doses of Co-60 (8.5-10 Gy, dose rate 0.25 Gy/min).

Acetato DL-α-tocopherol (50mg/kg body weight) using corn oil as carrier was orally administered to mice inmediately after exposure and 4 and 7 days later. Animals treated with only corn oil served as control.

Damage was assesed using mortality as endpoint. Animals were observed daily from the first day following irradiation. A group was sacrified at different times, and the other one when terminally moribund. Splenic weight and bone marrow and splenic cellularity were evaluated at different times (3-8-16-23 and 30 days). Body weight was daily monitored.

Data represent mean values obtained from 4 separate experiments and were analysed using Student t test.

RESULTS

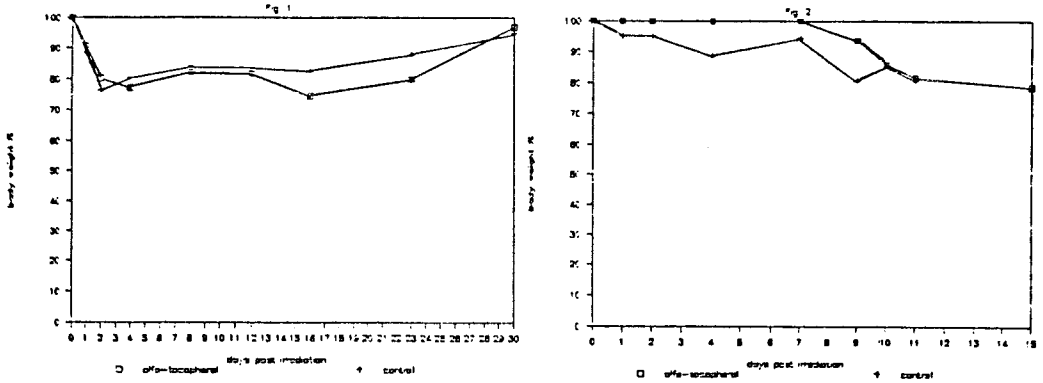
Survival data are summarized in Table 1.

SURVIVAL TABLE 1

	DOSE = 8.5 Gy		DOSE = 10 Gy	
day	α-tocopherol	control	α-tocopherol	control
0	100.0%	100.0%	100.0%	100.0%
7	97.6%	85.4%	100.0%	84.2%
10	84.6%	81.1%	100.0%	52.9%
14	61.1%	57.1%	11.8%	0.0%
30	21.2%	32.2%	0.0%	

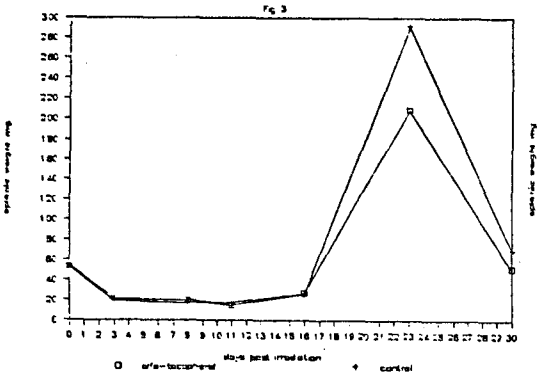
The α-tocopherol and control groups irradiated with 8.5 Gy showed a significant mortality by the 30 day, but up to 14th day α-tocopherol treated group had greater survival than control one. Although a dose of 10 Gy resulted in 100% lethality of treated and control animals by day 15 after irradiation, treated group had a significantly higher survival than control one up to 10th day.

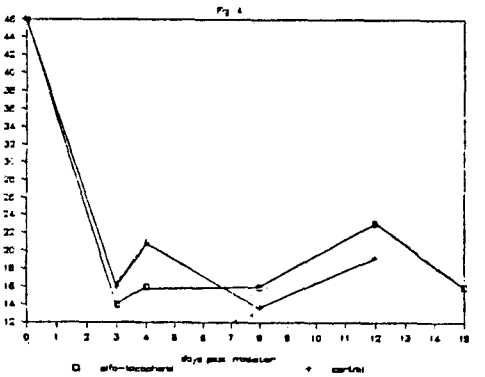
The body weight was decreased by about 20% on day 2 postirradiation in treated and control groups irradiated with 8.5 Gy. The growth recovered to the normal level by 30 days (fig. 1). Animals irradiated with 10 Gy did not reach normal weight until the end of the experience. Although the values are not significant, body weight in α-tocopherol treated group tended to be greater than control one (fig. 2).



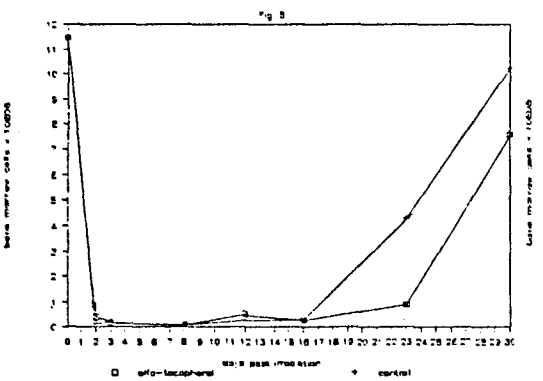
Relative to normal (nonirradiated mice) the splenic weight of 8.5 Gy irradiated animals was reduced to ≈30% at day 3 postirradiation and so on up to day 20, when it was observed an overshoot. Thirty days were needed for recovery to the control level (fig.3). A similar initial fall was observed in mice irradiated with 10 Gy. The splenic weight in α-tocopherol treated group tended to increase showing a

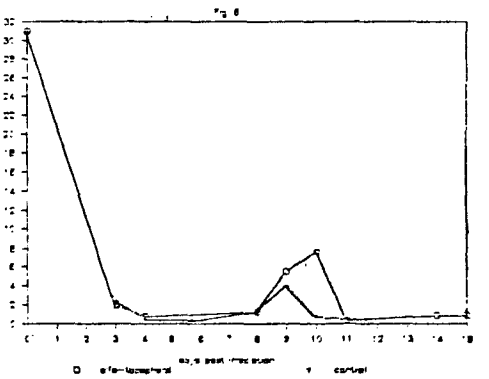
significant difference on day 12 ($p<0.01$). The splenic hyperplasia and the recovery to normal level could not be observed because of the earlier death (fig..4).





The bone marrow cellularity of both irradiated groups (8.5 Gy) reached minimal values (about 1.5% of the nonirradiated mice) on day 3, and tended to recover on day 12. The complete recovery was reached on day 30 (fig.5). Bone marrow cellularity of both irradiated groups (10Gy) decreased significantly to 0.7% on day 4, and turned to increase thereafter, but finally the recovery failed. However, mice treated with α-tocopherol exhibited increased bone marrow cellularity at day 10 postirradiation relative to control group (fig.6).





Qualitatively splenic cellularity was similar to bone marrow cell counts. However in groups irradiated with 8.5 Gy it was observed a very significant increase on day 20 postirradiation, reaching normal values on day 30, accordingly to splenic weight.

DISCUSSION

Although radiation lethality does not seem to be greated affected by the oral intake of α-tocopherol after irradiation our results show a greater survival in α-tocopherol treated groups up to 14th day and up to 10th day with doses of 8.5 and 10 Gy respectively.

After total body irradiation at low doses death from hematopoietic depletion continues beyond 10 .day, and is complete by 15 days, while death from gut failure occurres by day 10 at high doses.

Analysis of our data would suggest a probable radioprotector role of α-tocopherol on bone marrow syndrome. With doses of 8.5 Gy, the differences between bone marrow and splenic cellularity in α-tocopherol and control groups were not significant, but the survival of α-tocopherol treated group was higher than control one up to 14th day. In animals irradiated with doses of 10 Gy, it was observed not only a higher survival up to 10th day, but also bone marrow cellularity was greater in α-tocopherol treated group respect to control one. Alfa-tocopherol administered after irradiation would help animals exposured to recover from radiation damage, decreasing lipid peroxidation events. It is suggested these events are the result of a late metabolic disorganization caused by the radiation sickness.

Although our data are not concluding they show a trend to a radioprotector role. There would be diferent explanations for these not concluding results: 1) Alfa-tocopherol contained in corn oil (1mg/g corn oil, Rowe and Wills, (2)) could play certain radioprotective action, explaining why there were not significant differences in animal survival and bone marrow cellular counts with doses of 8.5 Gy. 2) The days chosen for the reinforcement doses of α-tocopherol probably were not accord to a 10 Gy dose of radiation, being the plasmatic levels of α-tocopherol not sufficient to prevent secondary lipid peroxidation events. 3) Alfa-tocopherol treated group irradiated with 10 Gy had higher survival and bone marrow cellularity at day 10. However, this dose resulted in 100% lethality by day 15. It could be suggested that this mortality is caused by gastrointestinal damage rather than bone marrow failure. It seems that α-tocopherol would prevent death from bone marrow depletion but not from gastrointestinal injury.

REFERENCES:

1- Rejholcovà, M. and Wilhelm, J., Rad. Research, 117:21-25 (1989)

2- Rowel, L. and Wills, E. D., Biochem. Pharmac., 25: 175-179 (1976)