Bulgarian Journal of Veterinary Medicine (2010), **13**, No 2, 81–86

COMPARATIVE INVESTIGATIONS ON BLOOD ADRENOCORTICOTROPIC HORMONE AND CORTISOL CHANGES AFTER TOTAL BODY GAMMA IRRADIATION OF RABBITS AND PIGS AT 0.1 AND 0.5 GY

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Summary

Kecheva, R. Z., 2010. Comparative investigations on blood adrenocorticotropic hormone and cortisol changes after total body gamma irradiation of rabbits and pigs at 0.1 and 0.5 Gy. *Bulg. J. Vet. Med.*, **13**, No 2, 81–86.

Ionizing radiation and the pathways of its deleterious effects on living beings are still of interest for investigators. The purpose of the present study was to investigate the dose-dependent alterations in blood plasma adrenocorticotropic hormone (ACTH) and cortisol in two animal species with different radiosensitivity after total body gamma irradiation within the dose range 0.1–0.5 Gy. The experiments were carried out with 10 male 3-month-old White New Zealand rabbits and 10 male pigs (Big White×Landrace crosses) at the age of 45 days. All animals were submitted to external gamma irradiation at doses of 0.1 Gy or 0.5 Gy. The results for blood hormonal assays showed that the total body gamma irradiation of both species at doses of either 0.1 or 05. Gy altered the activity of pituitary and adrenal glands. Pituitary changes were mainly functional and transient, whereas the higher exposure dose resulted in mainly structural changes in adrenal glands manifested by insufficiency of cortisol-secreting cells. It could be affirmed that the radiosensitivity of pituitary and adrenal secretory cells was different as could be seen from ACTH and cortisol secretion after irradiation of two species at two different doses of gamma radiation.

Key words: ACTH, cortisol, ionized radiation, pigs, rabbits

INTRODUCTION

The effects of ionized radiation upon the different organs and tissues of living organisms are still an object of interest for many researchers.

The existing data reported the response of specific systems to radiation and concluded that observed events occurred either directly, or indirectly via a unknown mechanism (Mizina, 2002; Keenan *et al.*, 2003; Georgiev *et al.*, 2005). The data of Korotkevich (1998) for the radiosensitivity of endocrine system, including the pituitary gland-thyroid gland-pancreas-adrenal glands-gonads are rather controversial.

Robinson *et al.* (2001) studied the effect of exposure at various doses upon the adrenocorticotropic function of adenopituitary gland – a central unit in adaptation mechanisms, are interesting. It was assumed that after irradiation, the influx of adrenocorticotropic hormone (ACTH) from the pituitary gland in blood circulation was impaired. The irradiation of mice

at doses of 500 and 750 R resulted in altered pituitary activity. At the same time, changes in the functional activity of adrenal glands also occurred (Keenan *et al.,* 2003; Agha *et al.*, 2005;).

The available literature data (Shaparov *et al.*, 1990; Leboran-Jacobs *et al.*, 2004; Georgiev *et al.*, 2005), although revealing some facts for the response of pituitary and adrenal glands to irradiation, do not provide information about the dose-dependent events in these glands.

The purpose of the present study was to investigate the dose-dependent alterations in blood plasma adrenocorticotropic hormone (ACTH) and cortisol in two animal species with different radiosensitivity, after total body gamma irradiation within the dose range 0.1–0.5 Gy.

MATERIALS AND METHODS

The experiment was performed with 20 animals – 10 male 3-month-old White New Zealand rabbits and 10 male pigs (Big White×Landrace crosses) at the age of 45 days. Depending on the exposure dose and the species, the following experimental groups were formed:

- Group I – rabbits irradiated at 0.1 Gy (n=5);
- Group II – rabbits irradiated at 0.5 Gy (n=5);
- Group III – pigs irradiated at 0.1 Gy (n=5);
- Group IV – pigs irradiated at 0.5 Gy (n=5).

Blood samples for analysis were obtained in EDTA tubes from the ophthalmic sinus in pigs and the auricular vein in rabbits prior to the irradiation and by hour 2 and days 1, 3, 7, 15 and 30 after the irradiation. The pre-irradiation values served as control.

All animals were exposed to the ionizing factor under conditions ensuring the homogenous total body irradiation (gamma irradiation unit Rokus-M with ^{60}Co as a radioactive source).

Blood plasma ACTH and cortisol concentrations were determined by commercial radioimmunoassay kits (Mallinckrodt Diagnostika, Hennef, Germany).

The results were statistically processed by the Student's test to assess the significance of differences between average values. A non-linear regression analysis was used for calculation of correlation coefficients (Statistica v.6; SPSS v.13).

RESULTS

The obtained results about the time course of ACTH and cortisol after irradiation at 0.1 and 0.5 Gy showed that for the entire period (between post irradiation hour 2 up to day 30), the pituitary-adrenal system reacted with a biphasic increase in ACTH and cortisol concentrations with a first phase occurring between the 2nd hour and 3rd day, and a second one – between post irradiation days 15 and 30 (Fig. 1 and 2).

In the earliest post irradiation period (hour 2) both doses elicited increased plasma hormonal concentrations. Thus, in pigs, ACTH increased from baseline values of 315 ± 7.06 pg/mL (Group III) and 342 ± 7.66 pg/mL (Group IV) to 465 ± 10.42 pg/mL ($P \leq 0.01$) and 428 ± 9.59 pg/mL ($P \leq 0.01$), respectively by the 2nd hour. In rabbits, this increase was from 286 ± 6.41 pg/mL to 485 ± 10.04 pg/mL (0.1 Gy group; $p \leq 0.01$) and from 274 ± 6.14 pg/mL to 510 ± 11.42 pg/mL in the 0.5 Gy group ($P \leq 0.05$). By day 1, ACTH concentrations returned to normal in both species and both used dose rates, attaining even lower levels. On the background of these ACTH levels, blood cortisol ex-

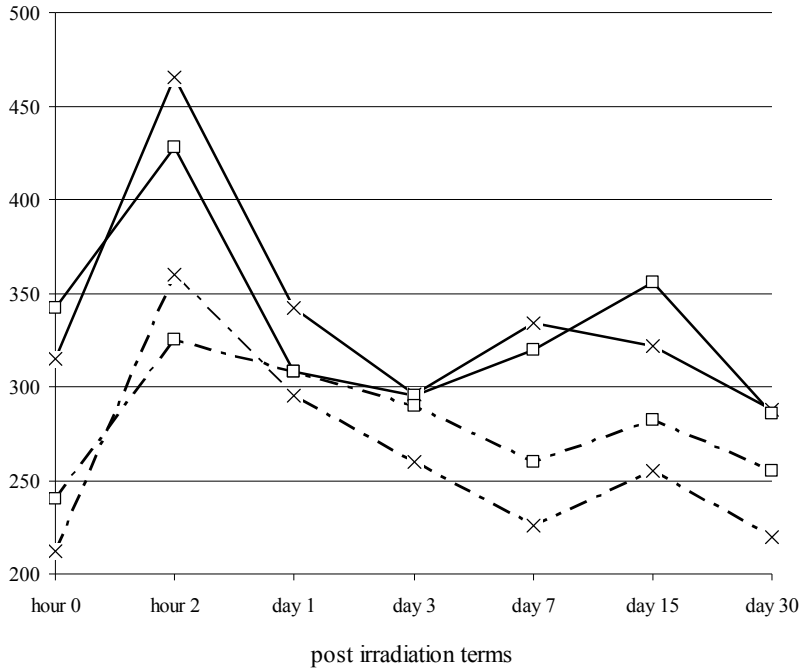

Fig. 1. Time course of blood ACTH and cortisol concentrations after irradiation of pigs at 0.1 Gy and 0.5 Gy. Legend: (—×—) ACTH+0.1 Gy; (—□—) ACTH+0.5 Gy; (- - ×- -) cortisol+0.1 Gy; (- - □- -) cortisol+0.5 Gy.

hibited increase in both pigs and rabbits as followed: from baseline values of 212 ± 4.75 nmol/L (0.1 Gy) and 240 ± 5.38 nmol/L (0.5 Gy), to 360 ± 8.06 nmol/L and 325 ± 7.28 nmol/l, respectively by hour 2 ($P \leq 0.01$). In rabbits, the change was statistically significant ($P \leq 0.05$) from 336 ± 7.53 nmol/L to 412 ± 9.23 nmol/L (Group I) and from 342 ± 7.66 nmol/L to 442 ± 9.90 nmol/L (Group II). These high cortisol concentrations persisted up to the 3rd day after the irradiation.

The regression analysis showed a positive correlation between the reaction of both glands (pituitary and adrenals) in both animal species studied (Table 1).

DISCUSSION

The total body gamma irradiation at 0.1 and 0.5 Gy resulted in biphasic increase in blood ACTH and cortisol in rabbits and pigs, similarly to the results of others (De Groot *et al.*, 2000; Georgiev, 2005). The first statistically significant elevation of ACTH occurred as early as the 2nd hour in both species as also shown by Pantic & Hristic (1975), Robinson *et al.* (2001), Georgiev *et al.* (2005).

The activation of pituitary hormone production and secretion lasted relatively shortly – up to the 1st day after the irradiation. Most probably, the short-time increase in ACTH was sufficient to induce a more prolonged activation of adrenal function, as confirmed by Litskevich (1995).

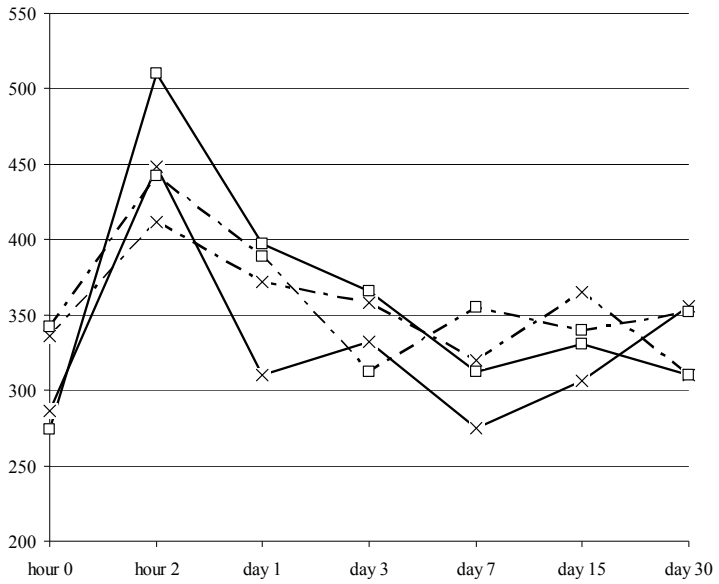

Fig. 2. Time course of blood ACTH and cortisol concentrations after irradiation of rabbits at 0.1 Gy and 0.5 Gy. Legend: (—×—) ACTH+0.1 Gy; (—□—) ACTH+0.5 Gy; (- - ×- -) cortisol+0.1 Gy; (- - □- -) cortisol+0.5 Gy.

Table 1. Correlation of blood ACTH and cortisol concentrations within a species after irradiation at 0.1 Gy and 0.5 Gy ($P<0.01$)

	ACTH 0.1 Gy	ACTH 0.5 Gy
Pigs		
Cortisol 0.1 Gy	0.896	
Cortisol 0.5 Gy		0.512
Rabbits		
Cortisol 0.1 Gy	0.635	
Cortisol 0.5 Gy		0.801

The adrenal cortex reacted to higher ACTH levels with increased blood plasma corticosteroid levels during the entire experimental period and vice versa, i.e. there was a positive correlation between the responses of both glands in the two studied species. Similar findings are reported by other authors (Leboran-Jacobs *et al.*, 2004; Litskevich, 1995; Georgiev, 2005).

In several reports, the existence of species-related differences in pituitary and adrenal hormonal secretion after irradiation is assumed (Litskevich, 1995; Korotkevich, 1998; Mizina, 2002). Analyzing blood ACTH and cortisol responses after irradiation at 0.1 and 0.5 Gy in this experiment, it could be asserted that the reaction of the pituitary-adrenal gland chain was comparable in rabbits and pigs. In both species, the changes in plasma concentrations of these hormones were similar although at a different extent for each specific time period.

It was therefore shown that the total body irradiation of two animal species (pigs and rabbits) at doses of 0.1 and 0.5 Gy, altered the activity of pituitary and

adrenal glands at a different extent. The blood concentrations of ACTH and cortisol allowed us to assume a different radiosensitivity for pituitary gland and adrenal glands with regard to the secretion of these hormones in the two animal species after exposure to different doses of ionizing radiation.

On the basis of experimental results, it could be concluded that pituitary changes were mainly functional and transient, whereas the higher exposure dose resulted in mainly structural changes in adrenal glands manifested by insufficiency of cortisol-secreting cells.

Although similar from a qualitative point of view, the quantitative changes in ACTH and cortisol demonstrated species-related differences. The reactions of pituitary gland and adrenal glands, as seen from the data on the quantity of secreted hormones, was stronger in pigs compared to rabbits, in which the changes were more gradual, especially after the 3rd day of irradiation at doses of 0.1 and 0.5 Gy.

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Paper received 10.04.2009; accepted for publication 20.11.2009

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