Hematological Changes Induced by Mercury Ions and Ionizing Radiation in Experimental Animals

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1. Introduction

Toxic metals such as lead, chromium, cadmium, mercury and arsenic are widely found in our environment [1]. Humans are exposed to these metals from numerous sources, including contaminated air, water, soil and food. Mercury, one of the most diffused and hazardous organ-specific environmental contaminants, exists in a wide variety of physical and chemical states, each of which has unique characteristics for a target organ specificity. Although reports indicate that mercury induces deleterious damage, little is known about its effects on living organisms.

Ionizing radiation, a extensively used therapeutic modality in oncology, not only eradicates neoplastic cells but also generates inevitable side effects for normal tissues [2]. Such biological effects are made through the production of reactive oxygen species which include a superoxide anion, a hydroxyl radical and a hydrogen peroxide. These reactive species may contribute to the radiation-induced cytotoxicity (e.g., chromosome aberrations, protein oxidation, and muscle injury) and to the metabolic and morphologic changes (e.g., increased muscle proteolysis and changes in the central nervous system) in animals and humans [3].

In the present study, radioimmunoassay of the cortisol in the serum and the analysis of the hematological components and enzymes related to a tissue injury were carried out to evaluate the effects of mercury chloride in comparison with those of ionizing radiation.

2. Materials and Methods

Fisher 344 male rats were used in the experiment. The rats were maintained under the following conditions; temperature (23℃) and lighting (12 hr light: 12 hr dark) and allowed free access to feed and water. Fifteen rats were allocated randomly into three groups of five rats each. Irradiated groups were exposed to gamma radiation from a ^{60}Co source (Panoramic Irradiator, AECL) with a total dose of 6.5 Gy, and a dose rate of 12.8 Gy/hr [4]. Mercury chloride was administered 1 mg/kg in the drinking water. All the rats were euthanized two weeks after irradiation. Immediately after death, blood was collected from the heart. Activities of GOT, GPT, LDH, and ALP were measured by using an automatic analyzer (Hitach, 747/200 type), which is based on the spectrophotometric quantification of the NADPH loss by using lactic dehydrogenase as a coenzyme [5]. Cortisol concentrations in the serum of the experimental groups were determined by a radioimmunoassay using Diagnostic Products (Diagnostic Systems Laboratories, USA) with a sensitivity of 8.28 nmol/liter [6]. The inter- and intra-assay coefficients of variation were < 8.3% and <10%, respectively.

3. Results and Discussions

This study was done to obtain the effects of mercury chloride in drinking water for whole body irradiated rats. The loss of the body and organ (liver, spleen and testis) weights in the irradiated rats was as expected (Table 1). However, the weights of the body and organ showed a rising tendency when compared to those of the control group.

Table 1. The weight of body and organs in the experimental groups (‡)

	CON	IRR	$HgCl_2$
Body wt	144.6 ± 0.73	123.8 ± 3.35*	151.6 ± 1.25
Liver wt	6.60 ± 0.23	6.07 ± 0.27*	6.83 ± 0.11
Kidney wt	0.84 ± 0.03	0.82 ± 0.02	0.77 ± 0.01*
Spleen wt	0.42 ± 0.003	0.25 ± 0.01*	0.43 ± 0.006
Testis wt	0.87 ± 0.02	0.58 ± 0.02*	0.89 ± 0.01

‡ , All values expressed as means ± SEM (n = 5).
*, $P < 0.05$ versus the control group.
Abbreviations; CON, control; IRR, irradiated group; $HgCl_2$, mercury chloride treated group.

The kidney weight increased to distinguishable values. It is suggested that the target organs of mercury chloride are the urinary organs. According to the hematological analysis, values of the RBC and platelets in the rats that were given mercury chloride increased markedly when compared to the control. These values, when compared to the irradiated rats, increased by 2.37 times and 4 times, respectively.

Hematological criteria of the mercury administered groups showed a similar pattern to those of the irradiated rats (Fig. 1).

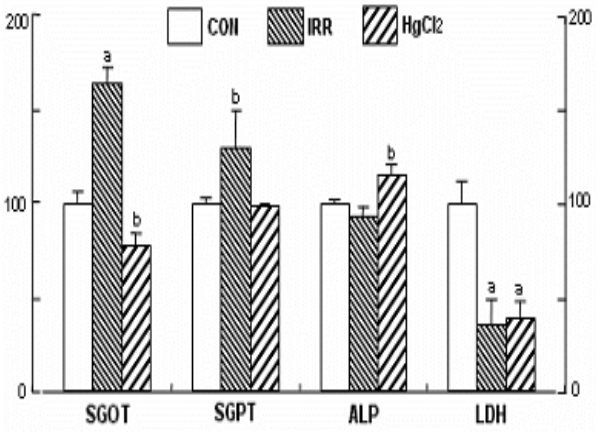

Figure 1. Ratio of serum glutamic oxaloacetic transaminase (GOT), glutamic pyruvic transaminase (GPT), alkaline phosphatase (ALP), and lactate dehydrogenase (LDH). a, $p<0.02$ and b, $p<0.05$.

Serum levels of the GOT and GPT indicated hepatocellular damage in the irradiated and mercury chloride-treated groups. ALP, an indicator of a renal injury, increased in the rats exposed to mercury chloride. Elevated levels of the circulating cortisol in both groups may indicate ACTH hypersecretion, adrenal dysfunction, and biological stress. Particularly, the ratio of the circulating cortisol of the irradiated rats increased higher than that of the mercury chloride treated group. It was shown in this study that mercury chloride induced a lesser damage than ionizing radiation.

4. Conclusions

Mercury chloride affects the organs including liver, kidney, spleen, and testis in the same way as ionizing radiation although the level of induced damage can be different according to its concentration. The main target organs of mercury chloride seem to be the urinary organs since it induced significant changes in the kidney weight and ALP levels.

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References

[1] D. van Veizen, H. Langenkamp and G. Herb, "Review: mercury in waste incineration". *Waste Manag. Res*., **20**(6), 556-568 (2002).

[2] H. Inano, K. Suzuki, H. Ishii-Ohba, Y. Imada, R. Kumagai, S. Kurihara and A. Sato, "Steroid hormone production in testis, ovary, and adrenal gland of immature rats irradiated in utero with ^{60}Co". *Radiat. Res*., **117,** 293-303 (1989).

[3] A. Maitra, I. I. Wistuba and A. F. Gazdar, "Microdissection and the study of cancer pathways". *Curr. Mol. Med*., **1**(1), 153-162 (2001).

[4] J. K. Kim, C. J. Lee, K. W. Song, B. R. Do and Y. D. Yoon. "Gamma-Radiation accelerates ovarian follicular atresia in immature mice". *In Vivo,* **13**(1):21-24 (1999).

[5] V. Lustig, A. Papanastasiou-Diamandis and D. M. Goldberg, „Evaluation of commercially formulated aspartate aminotransferase and alanine aminotransferase activity determinations by the Scandinavian Committee on Enzymes and IFCC methods as modified for use with automated enzyme analysers". *Clin. Biochem*., **21**(5):283-290 (1988).

[6] B. Kerdelhue, S. Brown, V. Lenoir, J. T. Queenan, G. S. Jones, R. Scholler and H. W. Jones, "Timing of initiation of the preovulatory luteinizing hormone surge and its relationship with the circadian cortisol rhythm in the human". *Neuroendocrinology* **75**(3), 158-163 (2002).