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THE SUBACUTE EFFECTS OF CADMIUM ON SEX HORMONES IN FEMALE RATS

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ABSTRACT

Toxic effects of trace elements upon the hypothalamic- pituitary-testicular axis and sex hormones have been reported in recent years. It is generally considered that $CdCl_2$ poisoning causes histopathological changes in the testicles of male rats. Little attention had been drawn to the possible toxic effects of $CdCl_2$ on the ovary and female sex hormones.

The purpose of the present study was to determine the subacute poisoning effects of $CdCl_2$ (10 mg/kg I.P. for 15 days) on the female gonadotropins and sex hormones such as FSH, LH, progestrone, estradiol and prolactin.

Female wistar rats 12 weeks of age (approximately 300g) were divided into two groups (10 in each group), one group received $CdCl_2$ and the other received saline as a control. Serum hormones were measured by radioimmunoassay.

In contrast to male animals, $CdCl_2$ injection did not affect serum FSH and LH concentration in female rats, whereas serum prolactin concentration was significantly elevated compared with that of control animals ($p<0.05$) after $CdCl_2$ injection. This effect is not similar to the effect of $CdCl_2$ on the prolactin of male rats which was reported by Chandler and coworkers. No marked differences were observed between the control and experimental values of serum estradiol and progestrone concentrations.

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INTRODUCTION

Trace elements, although found in very small amounts in the human body, are becoming of increasing interest in the field of biochemistry, physiology and nutrition, as well as many other developing fields. Although some of their mechanisms of action in human and animal metabolism are well known, detailed information about trace elements remains to be discovered.

Cadmium (Cd) ranks close to lead and mercury as a metal of current toxicological concern. It occurs in nature in association with zinc and lead, and extraction and processing of these metals thus often lead to enviromental contamination with Cd.[1] Workers in smelters and other metal- processing plants may be exposed to high concentrations of Cd in the air: however, for most of the population, exposure from contamination of food is most important. Shell fish and animal liver and kidney are among foods that have concentrations of Cd higher than 0.05 ug/g even under normal circumstances.[1]

Toxic effects reported with chronic exposure to Cd include kidney damage,[2] retardation of growth and hepatic damage,[3] inhibition of drug metabolising enzymes,[4] CNS damage,[5] reduced pancreatic secre-

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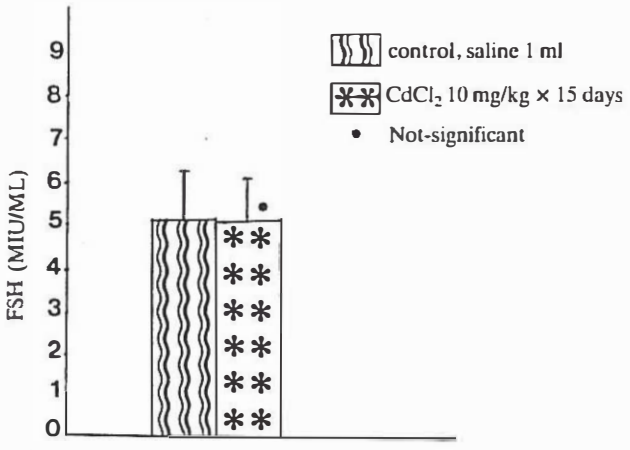


Fig. 1. The subacute effect of $CdCl_2$ on serum FSH in the female rat (n=30).

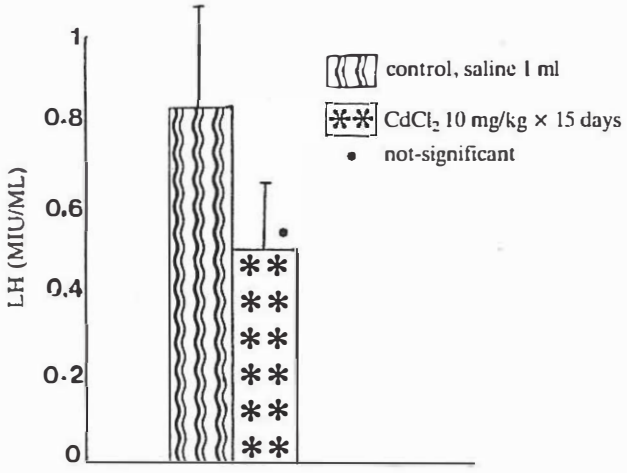


Fig. 2. The subacute effect of $CdCl_2$ on serum LH in the female rat (n=30).

tory activity,[6] renal dysfunction and hypertension[7] arteriosclerosis and cardiac disease.[8] Testicular necrosis due to Cd poisoning was reported for the first time by Parizek, et al.[9,10] Severe testicular damage in laboratory animals fed 10 mg/kg of Cd for one month was reported by Friberg.[11]

In recent years, toxic effects of trace elements upon the hypothalamic- pituitary- testicular axis and sex hormones have been reported by Sokol, et al[12] and Jianye, et al.[13] With regard to the influence of Cd on endocrine glands, it has been shown that Cd causes a decrease in serum corticosterone concentration,[14,15] a reduction in androgen synthesis and spermatogenesis,[16,17] and changes in thyrometabolic state.[17] Also Cd causes a prompt decline in FSH and an increase in serum LH levels of male rats.[18] Despite many studies of cadmium chloride ($CdCl_2$) on male reproductive organs and hormones, little attention has been drawn to the effect of $CdCl_2$ on female reproductive organs and hormones. It is only evident that $CdCl_2$ administration in hamsters induced inhibition of ovulation which was dose and time- dependent. The incidence of failure of ovulation was associated with decreased serum progesterone concentration.[19]

The purpose of the present study is to determine the possible subacute effect of $CdCl_2$ (10 mg/kg I.P. for 15 days) poisoning on the female sex hormones, namely FSH, LH, progesterone, estradiol and prolactin.

MATERIALS AND METHODS

Female wistar rats, 12 weeks of age (weighing approximately 330 g) were used. The animals were purchased from Pasteur Institute Tehran. They were kept in an air-conditioned animal room at about 25°C. $CdCl_2$ was dissolved in distilled water for intraperitoneal injections. Animals were divided into two groups (about 10 in each group). In the first group (controls), saline (1 ml) was injected intraperitoneally for 15 days. In the second group (experimental), animals were injected with $CdCl_2$, 12 mg/kg for 15 days I.P. At the end of 15 days, all animals were decapitated and all blood samples were collected between 8:00 and 9:00 a.m. Samples were left at room temperature to clot then centrifuged and sera were separated.

Serum concentrations of FSH, LH, progesterone, estradiol and prolactin in each sample were measured by radioimmunoassay procedures. FSH and LH in serum were measured by double antibody radioimmunoassay and concentrations of progesterone, estrogen and prolactin were determined by Coat- A- count radioimmunoassay. All samples were assayed in duplicate.

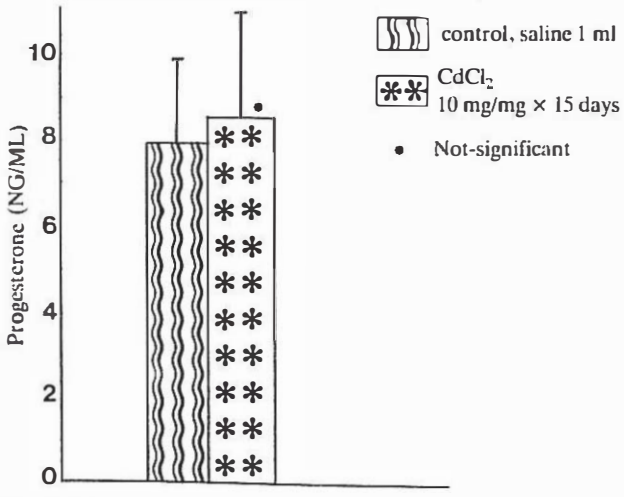


Fig. 3. The subacute effect of $CdCl_2$ on serum progesterone in the female rat (n=30).

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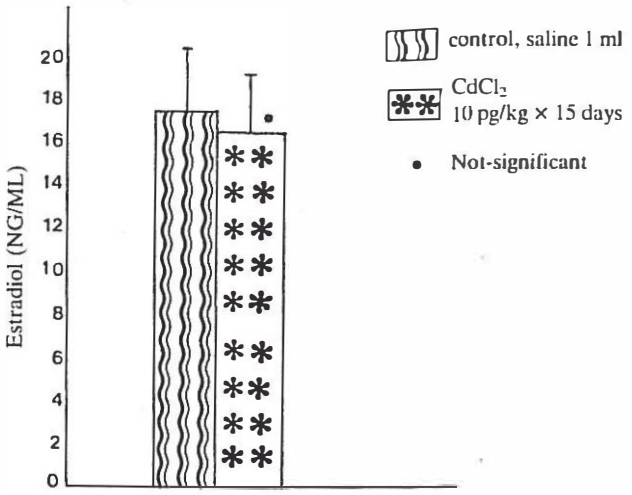


Fig. 4. The subacute effect of $CdCl_2$ on serum estradiol in the female rat (n=30).

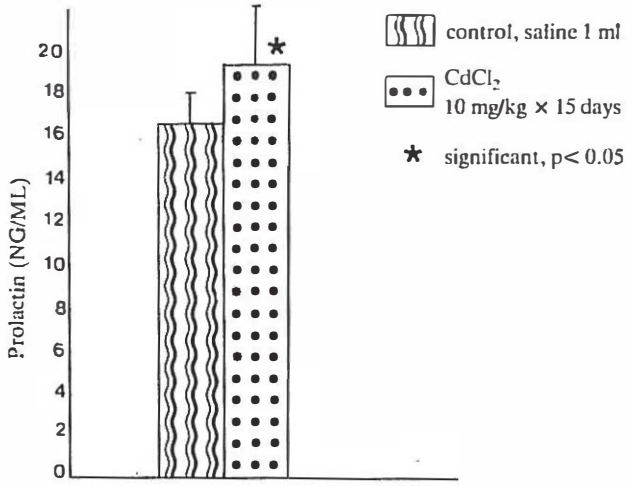


Fig. 5. The subacute effect of $CdCl_2$ on serum prolactin in the female rat (n=30).

Mean serum hormone concentrations of both groups were compared using student t- test. A value of $p< 0.05$ was considered to denote significant differences.

RESULTS

The serum concentrations of FSH, LH, progestrone, estradiol and prolactin were measured in both control and experimental groups. Results of radioimmunoassay analyses on serum hormone concentrations are summarized in Table I. The comparison between the mean serum concentrations of sex hormones and prolactin in both control and experimental groups are illustrated in Figs. 1-5.

The comparison between mean serum hormones concentration using t- test revealed no marked differences between the control and $CdCl_2$- treated groups' values for serum FSH, LH, progesterone and estradiol. In contrast, the serum concentration of prolactin in the $CdCl_2$ treated group was increased significantly ($p< 0.05$).

Table I. The effect of 15 days injection of $CdCl_2$ (10 mg/kg I.P.) on serum FSH, LH, progesterone, estradiol and prolactin concentration.

Animal group		Hormones				
		FSH miu/ml	LH miu/ml	Progesterone ng/ml	Estradiol pg/ml	Prolactin .ng/ml
Control	Mean ±SD	2.56 * ± 0.56	0.83 * ± 0.19	7.91 * ± 3.98	17.74 * ± 3.1	16.50 ‡ ± 1.37
Cd_2 Treated	Mean ± SD	2.53 ± 0.77	0.50 ± 0.13	8.58 ± 2.54	16.41 ± 2.8	18.65 ± 2.47

* = No marked differences were observed between the control and $CdCl_2$- treated groups' values for serum hormones x = Significantly different ($p< 0.05$).

DISCUSSION

Toxic effects of trace elements upon the hypothalamico- pituitary- testicular axis and sex hormones have been reported in recent years.[12,13] It is generally considered that $CdCl_2$ poisoning causes testicular damage[9-11] and histopathological changes in the testicles of male rats.[20,21]

With regard to influence on endocrine glands in the male rat, it has been reported that $CdCl_2$ causes reduced FSH, increased LH,[18] and decreased testosterone but has no effect on serum prolactin concentration.[14] Little attention has been drawn to the effect of $CdCl_2$ on the ovary and female sex hormones.

Effects of $CdCl_2$ on ovulation was reported by Saksena et al.[19] In addition it is reported that chronic exposure to Cd (5 p.p.m. in drinking water) increases preimplantation deaths and reduces serum progesterone in female rats.[22]

In contrast to males, $CdCl_2$ injection (10 mg/kg I.P. for 15 days) had no effect on serum FSH and LH concentration in female rats. Changes in serum FSH and LH concentration in males were thought to be caused by testicular damage and not by direct effect upon the pituitary.[19] Similarly, since $CdCl_2$ has no severe effect on the ovary, therefore it did not effect serum FSH and LH concentration.

Serum concentration of prolactin in the control and experimental groups was significantly different ($p< 0.05$) as the serum concentration of prolactin increased in the experimenal group. This result is not similar to the effect of $CdCl_2$ on the prolactin of male rats as

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reported by Chandler, et al.[16]

The exact mechanism and site of action of $CdCl_2$ toxicity on serum prolactin levels is not known. It is suggested that a predominant mechanism of action of Cd toxicity is at the level of the hypothalamic- pituitary axis. Antagonistic effects of divalent- cations such as Cd on the ovary or probably the pituitary prolactin receptor[23] may be a factor in increasing serum prolactin level in this experiment.

No marked differences were observed between the control and experimental values of serum concentration of estradiol and progesterone. This result is incompatible with decreased progesterone concentration caused by $CdCl_2$ (5 mg/kg S.C.) in hamsters reported by Saksena.[19] In that experiment, Cd was injected close to the time of LH surge on the day of proestrus. It is supposed that the cause of this incompatibility may be due to the time of Cd injection in estrus and time of sample taking in the experiments.

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