Cadmium Chloride Toxicity on Liver and Kidney of Albino Rat

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Abstract:

Cadmium is a naturally occurring non-essential heavy metal with no known positive biological function. It is present as a contaminant in food, water, and polluted air. Concern metal presents a serious threat to for both humans and animal health. Possible toxic effect of cadmium on general population exposed to low concentration over long periods of time has been raised in part because of its steadily increasing consumption and release in the environment. The present study was to effect of cadmium chloride on albino rats exposed to cadmium chloride.

Albino rats were exposed with low and high doses of cadmium chloride, along control. In two experimental sets, rats were treated for 30 and 60 days separately. In each of the experimental sets, Group A was control, Groups B exposed with lower dose of $CdCl_2$ (2.6mg/kg.b.wt.) and group C with high dose of $CdCl_2$ (5.2mg/kg.b.wt.). Study indicates significant increase ($P<0.05$) in the values of serum creatinine, urea, aspartate aminotransferase (AST) and alanine aminotransferase (ALT) while decrease in the values of alkaline phosphatase (ALP), cholesterol, and protein in the blood samples of animals exposed to different doses of cadmium chloride as compared to control when treated for 30 and 60 days.

Key Words: Cadmium chloride, liver, kidney, and enzymes.

Introduction:

Cadmium is a heavy metal present in nature in combined form. It is highly persistent environmental toxicant. It is present in air, drinking water as well as food and has potential to affect the health of human population; mainly those who live in highly industrialized regions (Sharrett *et.al.*, 1983, Smigiel *et. al*., 1994). Cadmium is considered as an occupational and environmental pollutant. As food chain contaminant, toxicity of cadmium is of great concern (MacLaughlin *et. al*. 1999; ATSDR, USA, 2012). Cadmium is present in cigarette smoke and polluted air, contributing to elevated cadmium concentration in blood urine and tissues of smokers, compared with non-smokers of similar age and gender (Satarug *et. al*. 2017)

Cadmium enters the body by various routs and get accumulated in various organs and organ system such as brain, liver, lungs blood system, bone, spleen, pancreas, and testes (Cai *et. al*., 2001; Emmanuel *et. al*., 2003). Cadmium toxicity is reported to be nephrotoxic (Jarup *et. al*., 2009), associated with generalized osteoporosis, osteomalacia (Horiguchi *et. al*., 2010) and type-2 diabetes (Satarug *et. al*., 2017)

Cadmium also has toxicological impact on plants and so their products for human consumption (Amir *et. al*., 2014). Intensive agricultural practices and industrial processing has resulted in the contamination of food, feed, and water, becoming source of exposure for humans. Some geographical areas are associated with the naturally occurring high cadmium concentration. Historically, rice consumption which being contaminated with cadmium from zinc discharge caused an outbreak of itai-itai disease affecting mostly women in Japan (Baba *et. al*., 2014).

Food and Agricultural organization (FAO) and World Health Organization (WHO) joint expert committee established guideline of a safe dietary cadmium intake and a urinary cadmium threshold limit. Currently dietary cadmium intake is within the FAO/WHO tolerable level of 58µg/day for 70 kg person (Soisungwan Satarug, 2017). But industrial pollution, other source of cadmium exposure like cigarette smoke, ingestion of polluted vegetables and ambient air in urban- industrialized areas (Gallagher *et. al*., 2004 and Thomas *et. al*., 2009) create a serious chronic exposure to heavy metals especially to cadmium. Asian subpopulations have been found to have the highest mean blood cadmium among five ethnic group studied in the U. S. National Health and Nutrition Examination Survey (NHANES 2011-2012). The aim of this study was to investigate the toxic effects of chronic and sub chronic cadmium exposure on hematological and biochemical parameters in albino rats. Experimental results will act as biomarker in the cadmium toxicity.

Material and Methods

Experimental Animals

Albino rats of 6 to 10 weeks old weighing 150- 160 grams were purchased from the Laboratory Animal Resource Section, of Indian Veterinary Research Institute (IVRI) Izzat Nagar Bareilly, U.P. that were maintained in experimental animal shed of the division. Animals brought into new conditions were acclimatized to the new environment prior to the experiments. Rats were kept under conventional condition (6 rats per steel cage, 12 hr. light to dark cycle) and were maintained with standard rat food and tap water *ad libitum.* All the chemicals used were from the Sigma Chemicals Co., Merk and Qualigens.

Experimental Design

The experimental rats were randomly divided into three groups A, B, and C each comprising of 6 animals. Group A was control remaining two groups were intoxicated with different chronic doses of heavy metal (Cadmium chloride) compound, Group B Cadmium chloride (low dose) with 2.6 mg/kg.b.wt, Group C with Cadmium chloride(high dose) 5.2 mg/kg.b.wt The compounds were given in tap water as they were easily soluble in it while the control received only plain tap water per os by gavage. Rats under the above treatment were monitored for 30 days and 60 days and their body weight were taken weekly. Mortality rate, food consumption, clinical signs and symptoms and behavioral activities were under observation.

Blood was collected for hematological and biochemical examination after 30 days and 60 days from the retro-orbital plexus with the help of capillary tube as described by Sorge and Buckner (1964). Blood was collected in two aliquots. In one aliquot, EDTA(1mg/ml) was added for hematological parameters estimation other aliquot was without any anticoagulant for harvesting serum for biochemical estimation (centrifuged at 3000 rpm for ten minutes). The test samples were stored in air vials at -20^{o}C till used.

Statistical analysis

All data presented as the mean ±standard error of mean (SEM). The results were analyzed for statistical significance by one-way analysis of variance (ANOVA) followed by Dunnett's *post hoc* test of significance. *P* values less than 0.05($p \leq 0.05$) were considered as statistically significant.

Result and Discussion

Clinical observations showed that exposed animals were docile and less active than control group. No mortality occurred in control and other groups treated with the different doses of heavy metal. There was time and dose-dependent reduction in the body weight when treated for 30- and 60-days duration. The effect of treatment of cadmium chloride on different organs of albino rats when intoxicated for 30 days and 60 days is given in Table 1 to 2.

Table 1: Blood biochemical profile after oral administration (gavage) of cadmium chloride for 30 days.

Group	AST (IU/L)	ALT (IU/L)	ALP (IU/L)	Creatinine (mg/dl)	Cholesterol (mg/dl)	Urea (mg/dl)	Protein (g/dl)
Group-A: Control	39.5±1.21	28.1±0.28	57.00±0.40	0.65±3.53	20.22±1.52	29.6±1.6	7.44±0.19
Group-B: Cd (L)	40.4±0.96	31.2±0.91	46.02±0.72	0.67±1.15	17.08±2.69	31.9±1.51	6.50±0.62
Group-C: Cd (H)	41.9±2.03	36.2±2.15	39.41±0.40	0.85±1.06	16.46±3.27	35.04±2.1	6.18±0.52

●Cd (L) = Cadmium Chloride Low Dose ●Cd (H) = Cadmium Chloride High Dose
●All the values are mean±SE; n=6

Blood biochemical parameters of animals receiving cadmium chloride for 30 days, showed significant increase in the values of AST, ALT, creatinine, and urea. Group C increase showed more significant increases in AST (6.07%), ALT (28.82%), creatinine (30.76%) and urea (18.37%) as compared to control. On the other hand, ALP, cholesterol, and protein values showed marked decrease from 16.9% to 30.8% in these parameters. It was strange to see fall in ALP.

In the second set of experiment for 60 days the AST, ALT, creatinine, and urea values showed the same trend of increase in cadmium intoxicated groups i.e., Group B and Group C. Animals of group C with high dose of cadmium showed increase of 5.7% in AST level, 37.8% in ALT, 40.84% in creatinine and 37.26% in urea when compared to control group A. Cholesterol, ALP, and protein showed decrease in both the treated group compared to control. Fall of 44.77% in ALP, 24.44% in cholesterol and 10.6% in protein was observed. Group B showed less fall when compared to group C with high cadmium dose. Decrease in different liver and kidney biomarker parameters, was dose and duration dependent. These observations shows that cadmium produced toxic effect on body hampering the function of liver and kidney.

Table 2: Blood biochemical profile after oral administration (gavage) of cadmium chloride for 60 days.

Group	AST (IU/L)	ALT (IU/L)	ALP (IU/L)	Creatinine (mg/dl)	Cholesterol (mg/dl)	Urea (mg/dl)	Protein (g/dl)
Group-A: Control	40.1±1.46	30.1±0.24	54.92±1.50[a]	0.71±1.08	20.95±0.44	30.43±2.38	6.60±0.11
Group-B: Cd (L)	41.87±1.45	32.7±2.59	39.98±1.35[be]	0.89±2.31	18.69±1.58	33.75±1.86	6.28±0.33
Group-C: Cd (H)	42.4±2.5	41.5±2.3	30.33±1.71[bdf]	1.00±1.36	15.87±1.44	41.77±1.41	5.90±0.31

●Cd (L) = Cadmium Chloride Low Dose ●Cd (H) = Cadmium Chloride High Dose
●All the values are mean±SE; n

Clinical observations showed that animals were docile and less active than control. No mortality occurred in control as well as intoxicated groups with cadmium chloride. In treated group there was a dose-dependent reduction in body weight gain. Hematological and biochemical indices have been reported to be reliable parameters for the assessment of health status of animals and humans (Ohaeri *et. al.*, 2011). Toxic compounds affect the metabolism and function of mature blood cells and disturb hematopoiesis process. The response to toxic influences manifests itself primarily in reduction of the number of circulating blood cells along its functional and structural abnormalities.

Alteration in hematological parameters and activity of serum enzymes were frequently indicators of toxicity, organ damage and cell damage (Kodavanti and Mehendale, 1991). Production of cells in bone marrow is reported to be highly sensitive to toxic influences. Sometimes only one cell line is affected by toxic substances and sometimes all of them.

Many biochemical parameters are biomarkers to evaluate the possible toxic effect on liver and kidney caused due to disturbed physiological functions responsible for many diseases (Smaoui *et. al.*, 2000; Hannah *et. al.*, 2016). The result of study showed a significant increase in enzymatic activity of AST and ALT. Increased activity of these enzymes in blood represents their leakage of tissue into plasma following a hepatic lesion responsible for the deterioration of the membrane permeability (Layachi and Kechrid, 2012; Diaby *et. al.*, 2016) and characteristic white globules (Albasha and Azab, 2014) destroying cell of liver directly. It is also reported to be cellular lesion and pyknotic nuclei caused due to the cell necrosis in cadmium toxicity (Wakeel *et. al.*, 2020). Results of this study shows significant increase in the level of creatinine and urea compared the control, may be due to renal insufficiency (Guilhermino *et. al.*, 1998; Boujelbene *et. al.*, 2002). Kidneys are reported to be target organs of toxic effects of cadmium (Wang *et. al.*, 2014; Satarug, 2018) which accumulate here causing kidney damage (Poontawee *et. al*., 2016). Cadmium toxicity causes tubular dysfunction reducing glomerular filtration leading to kidney failure (Fahim *et. al*., 2012) disrupted nuclei, paler cytoplasm, and scanty chromatin.

Cholesterol, ALP, and plasma protein decreased in the treated animals was also reported by Guilhermino *et. al*. in 1998. Fall in ALP as biomarker might be associated to hepatobiliary injury. The decrease in plasma total protein, which seems to be attributed to decrease in albumin was also indicative of cadmium induced liver and kidney injury (Guilhermino *et. al*., 1998). Ferrao *et. al*. (2010) reported that blood cadmium is associated to impaired renal function and proteinuria (albuminuria). In United States population. Low cholesterol is associated with the lipid metabolic abnormality due to the cadmium toxicity agrees to the study by Saeed Samarghandian *et. al*. (2015), who reported that low cadmium concentrations ca adversely affects the lipid and lipoprotein profile is a lipid peroxidation. Zhou *et. al.* (2016) reported that cadmium exposure is associated with dyslipidemia.

Conclusion

The results obtained from the present study indicates that cadmium toxicity, in two different sub chronic doses, induce alteration in blood biomarker enzymes of liver and kidney. Increase in AST, ALT, creatinine, and urea showed that cadmium produces toxic effects on liver and kidney. Low cholesterol, ALP, and blood protein was observed. Thus, the study shows that cadmium as environmental pollutant is hazardous to human and animal health. Monitoring the level of these heavy metal contaminant in eatables, drinking water and occupational exposure, humans can be saved from disease and ill health leading to sustainable environment.

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