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Induction of Testicular Degeneration syndrome via Cadmium Chloride in male Albino rats

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Abstract

This study was designed to induction of testicular degeneration syndrome (TDS) in male rats by cadmium chloride and identified the best concentration of induction for this syndrome.

The effective dose of cadmium chloride ($CdCl_2$) was determined by used fifteen males rats and where divided into three equal groups treated with $CdCl_2$ in a concentration (1, 2 and 3) mg/kg B.W. I.P. one /week for two weeks. Later the experimental animals was scarified and testis was took for measuring the antioxidant parameters via evaluated of glutathione GSH, malondialdehyde MDA, catalse, albumin, fructose concentrations and aminotransferase activity (ALT and AST).

According to this result the lowest observed adverse effective dose (LOAEL) of cadmium chloride that induced testicular degeneration in male rats was found to be 1mg/kg B.W. I.p. one /week for two weeks.

Key word: cadmium chloride, testicular, degeneration

Introduction

Heavy metals' toxicity is considered to be one of the major threats to healthy life. The degree of toxicity is mainly assigned to solubility and absorption status [1]. Cadmium in its elemental form occurs naturally in the earth's crust and it is unusual to find it in its pure form [2]. It is commonly found in combination with other element such as oxygen (cadmium oxide), sulfur (cadmium sulfate[, chloride)cadmium chloride[, and carbon (cadmium carbonate) and cannot be degraded or destroyed, which can be enters the body through contaminated water, air, and food, ingestion of contaminated soil or dust as well as in 40-60% of the cadmium content in cigarette smoke. As a result, smokers receive a dose of cadmium daily and generally have cadmium blood levels 4-5 times more than those of nonsmokers [3]. The toxicity of cadmium was first described by Friedrich Stromeyer in 1817. In the 1940s, environmental exposure to cadmium's toxicity was reported in Japan's Jinzū river basin, where a disease called itai-itai tormented many people, these patients showed a wide range of symptoms, such as low-grade bone mineralization, a high rate of fracture, an increased rate of osteoporosis and intense bone-associated pain. This affliction occurred because the river basin's inhabitants had consumed local rice, which had been grown in fields irrigated with cadmium-contaminated water [4]. Several factors can increase this uptake, such as low intake of vitamin D, calcium and iron cadmium can be absorbed into the body through the gastrointestinal, respiratory and dermal systems. It has been demonstrated that cadmium uptake in people with anemia and habitual iron deficit, such as children or menstruating women, is higher than in other people. It binds to biological macromolecules like proteins and some other compounds, such as metallothionein and sulfhydryl-containing molecules are responsible for the protection of repair systems in living cells against free-radical-induced cell damage [5]. That Cd toxicity stimulates the production of reactive oxygen species [ROS[such as superoxide ions, hydroxyl radicals, and hydrogen peroxide and the induction of oxidative stress in different organs. These radicals are able to oxidize biological macromolecules, particularly proteins, DNA and altered gene expression results in structural perturbations and subsequent metabolic disorders [6]. Moreover, Cadmium exposure stimulates lipid peroxidation-induced tissue damage and injury. cadmium chloride affect specific organs, kidneys, spleen, bone, and liver, pancreas, thyroid, salivary glands, bone and central nervous system, most frequently testes [7]. It then circulates in the blood and reaches tissues such as testis, where it is accumulating and disrupting the blood-testis barrier, comes into close contact with different cells of testis [8]. It has been reported that cadmium salts like cadmium chloride cause sterility in adult rats, mice, and hamsters via increased numbers of apoptotic spermatid and elongate spermatid in seminiferous tubules of rats, they also discovered severe necrosis of the seminiferous epithelium itself due to a high level of peroxidation in lipid membrane of testicular cell [9 and 10].

So that . This study was designed to induction of testicular degeneration syndrome (TDS) in male rats by cadmium chloride and identified the best concentration of induction for this syndrome.

Materials and Methods

Ethical Approvals:

The consent was taken from the Central Committee for Bioethics University of Kufa, Informed and written consents were obtained from all participants.

to determination the concentration of cadmium chloride ($CdCl_2$) that induced testicular degeneration syndrome due to various and wide range of concentration and experimental day in different studies and the critical toxic concentration of $CdCl_2$. By used nine males rates divided into three equal group treated $CdCl_2$ in a concentration (1, 2 and 3) mg/kg body weight intraperitoneal injection (IP). one /week for two weeks the studies parameters were measured testicular tissue antioxidant parameters reduced glutathione (GSH) concentration, malondialdehyde concentration (MDA[, catalase concentration, albumin concentration, fructose concentration and testicular tissue aminotransferase activity ALT and AST) also the testicular tissue will be taken for histopathological examination would be measured. According to result of measured parameters the lowest observed adverts effect level (LOAEL) of cadmium chloride that induced testicular degeneration syndrome in male rats was equal to 1mg/kg B.W. I.P. one /week for two weeks.

Statistical analysis

Statistical analysis of the experimental results was conducted according to Graphpadprism8. Used to assess the significance of differences between groups and within times. The data were expressed as mean ± standard errors ([SE) and (P value<0.05) was considered statistically significant LSD was carried out to test the significant level among the means of treatments (Prism., 2019).

Result and Discussion

The data presented in figure (1A,B,C and D)[demonstrated that I.P injection of CaCl2 in concentration of 1,2,3 mg/kg B.W once/week for two-weeks interval showed that graded decrease in testicular tissue parameters include reduce glutathione, catalase, albumin, fructose concentration, aminotransferase enzymes ALT,AST and increase malondialdehyde concentration MDA in all treated group, meanwhile the lowest observed adverse effective dose (LOAEL) of CaCl2 that induced testicular degeneration syndrome without lethal effects in males rats was found to be equal to 1mg/kg B.W once/weeks IP,

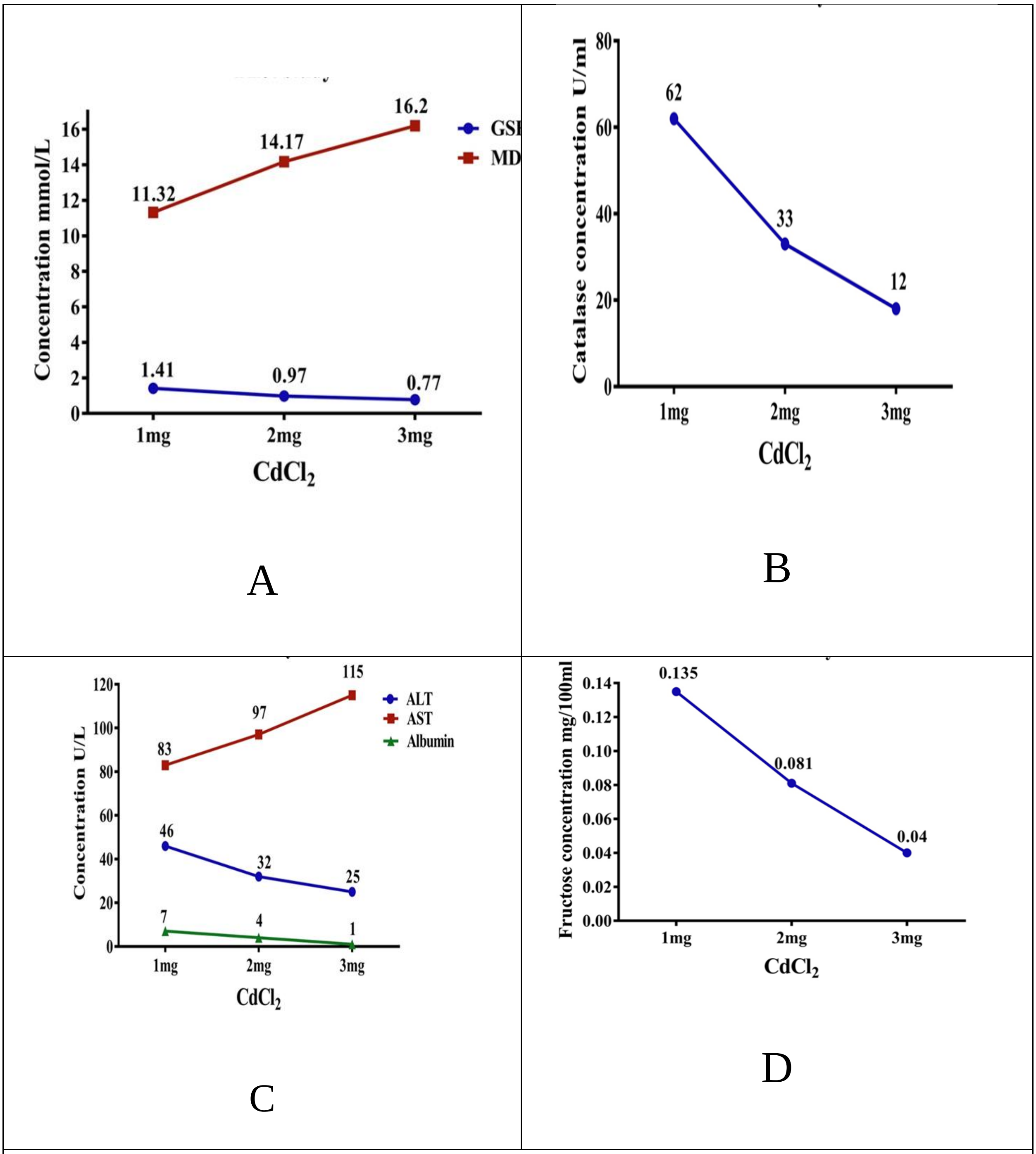

Figure [1[: Testicular tissue glutathione ,(A): malondialdehyde concentration (MDA concentration) (B):catalase, (C): albumin, aminotransferase enzymes (ALT,AST) and (D): fructose concentration in cadmium chloride injected male rats.
-Values are expressed as the means and error bars represent standard error (SE).
-Induction = animals injected with CdCl2 1mg/kg B.W. I.P. once /week for two weeks.
- * Denote differences between groups, P<0.05

Several studies have revealed that CdCl2 causes cytotoxicity and alteration of antioxidant capacity and aminotransferase activity linked with testicular dysfunction, thus causing changes in the histological of testis through induced oxidative stress by enhancing the production of reactive oxygen species [ROS[, in the testis may lead to further injury to vital components of the cell which cause serious damage to the reproductive system cells and development of male infertility. Cd binding to sulfhydryl groups SH groups from cell membrane proteins, cytoplasmic proteins and enzymes lead to increase lipid peroxidation in the cell membrane can disrupt fluidity and permeability of cell membranes and damage all cells [11][.

In other words, when the cell membranes are damaged by free radicals, their protective cell is lost and thus the total cell is exposed to risk. In this regard, increased production of ROS induces lipid peroxidation in testis. MDA is produced due to the degradation of the peroxides of unsaturated fatty acids. It is used as a biomarker to determine the rate of oxidative damage to lipids, the damage caused by lipid peroxidation is the most important factor for testicular dysfunction and changes in the antioxidant defense system lead to decrease in intracellular glutathione, catalase, albumin and fructose concentrations in the testes [12] Membrane integrity decreased, mostly in the part of the mitochondrial after cadmium exposure to spermatozoa [13]. It also affects the ubiquitin adenosine triphosphate (ATP) depend on the proteolytic pathway, which ATP is the most important energy source for sperm motility. Seminal fluid contains high concentration of fructose [14] and has important role in functional properties in sperm since scientists suggested that plays multifaceted and important role as an energy source for sperm metabolism and motility, deficiency causes abnormal sperm formation and irregular motility development [15].

Among the mechanisms of toxicity of CaCl2 on testes is a failure in blood circulatory because of vascular damage and drop in fructose utilization by spermatogenic cells in the spermatogenesis process due to action of cadmium which is competitive to fructose. Normal seminal fructose concentration confirms the role of testosterone and the function of vesicles and vas deferens are normal [16]. Overall, in the present study, the results that percent in figure [1] indicated that CaCl2 causes reversible testicular degeneration after 14 days which show decreased in testicular tissue antioxidant parameters include glutathione, catalase, albumin, fructose, ALT, AST and increase MDA or lipid peroxidation. All these results were in accordance prior studies which found that CaCl2 causes significantly decreased in all testicular tissue antioxidant parameters and aminotransferase concentrations and after 15 to 30 days of exposure to CdCl2 which cause destroyed the testis, Leydig and Sertoli cells, also caused increasing the death of cells and reduction in the germinal layer which decrease the thickness in the seminiferous tubules[17 and 18].

Cadmium chloride changing the gross antioxidant mechanisms which that leaded to the oxidative damage. Therefore, CaCl2 causes damage in DNA and protein, all of these by increase in lipid peroxidation. At lower CaCl2 dose the effects of oxidative damage effect on germ cell, which destroyed the spermatogonia [19]. However, the toxic effect of CdCl2 became considerable reduction of these parameters in all effective concentrations which increased the lipid peroxidation indicated the harmful effect of cadmium on the testicular structures and membrane integrity as showed in rabbit [20], bull [21 and 22] and human [24] when used the cadmium chloride in different effected dose. In the result showed that significant decrease in antioxidant enzymes and increase lipid peroxidation or MDA concentration due to effect of CaCl2 after 14 days of injection intraperitoneally according to our pilot study in dose 1 mg/kg body weight. These findings were similar to those reported from animal studies by uses CaCl2 orally given at 5 mg/kg BW. for 30 days in rats [25], by effective injection of CaCl2 in mouse [26], in goat sperm [27] and research involving humans [28] .

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