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Protective effects of selenium against cadmium induced hematological disturbances, immunosuppressive, oxidative stress and hepatorenal damage in rats

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ABSTRACT

Cadmium is a non-essential toxic metal used in industrial process, causes severe risk to human health. Selenium (Se) is an essential trace mineral of fundamental importance for human health. Selenium has antioxidant enzymes roles and is needed for the proper function of the immune system. In this study, the protective effects of selenium against cadmium intoxication in rats have been investigated by monitoring some selective cytokines (IL-1β, TNF α, IL-6, IL-10 and IFN-γ), antioxidant enzymes reduced glutathione (GSH), superoxide dismutase (SOD), catalase (CAT), glutathione peroxidase (GPx) and lipid peroxidation malondialdehyde (MDA) as well as some selective biochemical markers of liver and kidney functions. Thirty-two rats were divided into four equal groups; the first group was used as a control. Groups 2–4 were treated with selenium (Se; 0.1 mg/kg BW), cadmium (Cd; 40 mg/L drinking water) and selenium plus cadmium, respectively. Rats were orally administered their relevant doses daily for 30 days. Blood samples were collected from heart puncture at the end of the experiment (30 days) for complete blood picture (CBC) and serum was separated to evaluate the different immunological parameters and biochemical parameters, as well as liver specimens for Cd and Se estimation. Rats in the Cd treated group have a significantly higher hepatic concentration of Cd than in other treated groups. Results revealed that cadmium significantly increased IL-1β, TNF α, IL-6 and IL-10, beside peripheral neutrophils count, while the IFN-γ and lymphocytes were decreased in rat sera. In addition, GSH level, CAT, SOD and GPx activities were significantly decreased while lipid peroxidation (MDA) was increased. Regarding, liver and renal markers, they were significantly increased in the activities of aminotransferases (AST, ALT), urea and creatinine, while total plasma proteins and albumin were significantly decreased. On the other hand, selenium treated group, showed significantly increased IFN-γ, GSH level, CAT, and GPx activities, as well as lymphocyte count while IL-10 was decreased. Selenium in combination with cadmium, significantly improved the elevation of serum IL-1β, IL-6, TNF α, IL-10 and malondialdehyde in addition to enhancing the antioxidant enzyme activities of GSH, CAT, GPx and SOD. Moreover, selenium has ameliorated the cadmium-induced liver and kidney damage by improving hepatic and renal markers. The results of this investigation demonstrated that selenium has the potential to countermeasure the immunosuppressive as well as hepatic and renal oxidative damage induced by cadmium in rats; selenium has shown promising effects against Cd toxicity.

Introduction

Adverse immune effects of chemicals, defined as immunotoxicity, has been used as a sensitive biomarker for assessing health effect of environmental pollution. Immunotoxic effects of non-essential toxic metal, as a typical environmental agent and their mechanism are areas of interest. Cadmium (Cd) is one of the most

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toxic non-essential toxic metal, an environmental and occupational pollutant endangering human and animal health [1,2]. It has been suggested that Cd may be an environmental risk factor for osteoporosis and fertility as well as nephrotoxicity, hepatotoxicity, and immunosuppressiveness [3–7]. The immunotoxic effects of Cd on the development of immune organs, the differentiation of immune cells, and specific and non-specific immune responses have been reported by Koller [8]. This indicates an impact on the immune system as a whole, which can lead to a significant decrease in host resistance. Moreover, some of the specific changes that lead to tissue damage and death from chronic exposure to Cd have been related to oxidative stress [10]. The associated toxic effects of cadmium attributed to suppression of free radical scavenging function and the enhancement of ROS contribute to Cd induced oxidative stress and lipid peroxidation [10–12].

Selenium (Se) is an essential trace element for both animal and human begins. It has been detected that selenium function through participates in formation of selenoproteins, this element contributes in various biological processes such as antioxidant defense, thyroid hormone production, and immune responses [13,14]. Some reports indicate that a deficiency in selenium may be flat to certain diseases [15]. It is generally recognized to be of great importance for human health, protecting the cells from the harmful effects of free radical production [16]. Adverse health effects following selenium overexposure, although very rare, have been found in animals and people [15]. Selenium interaction with cadmium has been reported; this interaction may reduce cadmium accumulation and subsequent reduce its toxicity in the body [15]. Although many of the studies that have been carried out until now reported on the different adverse health effects of Cd, such as its nephrotoxicity, hepatotoxicity, and immunosuppressiveness, however, none has dealt with the association between cadmium and selenium. Therefore, the present study was conducted to shed some light on the relationship between the immunosuppressive, renal and hepatic damage, hematological disturbances as well as oxidative stress effects of cadmium and the putative protective effects of selenium in rats.

Materials and methods

Experimental animals

The experiment was conducted in accordance with animal welfare and under ethical protocols by the Faculty of Veterinary medicine, Mansoura university, Egypt. Forty rat weight (160 ± 10 g), housed in a plastic cages 50 cm × 30 cm × 10 cm and placed in the room for 10 days for adaptation. The room temperature was maintained at $24 \pm 2\,^{\circ}$C, the air of the room was changed continuously by using ventilated vacuum and with light\dark cycle of 12:12 h per day. The animal was fed on a pellet diet.

Chemicals

Sodium selenite (Na_2SeO_3) and cadmium chloride anhydrous ($CdCl_2$), which were analytical grade (≥99%) and were obtained from the Sigma Aldrich Chemical Co. (St. Louis, Missouri, USA). All chemicals and reagents used in this study were of analytical reagent grade.

Experimental design

Thirty two male albino rats were involved in this study. Rats were randomly divided into four groups of eight rats each; the first group was used as a control. Groups 2 and 3 were treated orally with Se (0.1 mg/kg BW), and cadmium 40 mg/L in drinking water, respectively, for 30 days. The cadmium dose used in the present study used according to published literature procedures [17]. Group 4 was orally administered Cd at doses of 40 mg/L and Se at a dose of 0.1 mg/kg BW.

Samples collection and parameters measured

The blood samples were collected in test tubes contained disodium salt of ethylene diamine tetra acetic acid (EDTA) anticoagulant and used for determination of red blood cell counts (RBCs), hemoglobin (Hb) concentration, Hematocrit (HCT) and erythrocyte indices, mean corpuscular volume (MCV), mean corpuscular hemoglobin (MCH) and mean corpuscular hemoglobin concentration (MCHC), in addition, white blood cells (WBCs) and platelets (PLTs). Three blood films were made for each blood sample. Blood films were stained with Giemsa stain and differential leukocyte count was done by standard hematological techniques. The second blood samples were collected in test tubes without anticoagulant. The samples were centrifuged at 3000 rpm for 10 min and the clear serum was carefully separated from all samples. Selective humoral immunological parameters (Tumor necrosis factor – α (TNF α), Interleukin 1β (IL-1β), IL-6, IL-10 and gamma interferon (IFN-γ) were determined by Enzyme Amplified Sensitivity Immunoassay (EASIA, R & D Systems, Minneapolis, MN, USA) using microplates according to enclosed pamphlets (Aushon Searchlight Biosystem (Billerica, MA). The lower detection limits are 1.5 pg/mL for IL-1β, 6.3 pg/mL for IL-6, 5.4 pg/mL for IL-10, 3.1 pg/mL for TNFα, and 6.2 pg/mL for IFN-γ and data are presented as pg cytokine/mL serum.

Antioxidant markers, reduced glutathione (GSH), superoxide dismutase (SOD), catalase (CAT), oxidized glutathione, (GPx) and malondialdehyde (MDA), were determined from undiluted serum samples using commercially available ELISA Kits (Cayman Chemical Co.). The plates were read at 450 nm and a correction wavelength of 550 nm on a computerized automated microplate ELISA reader. ALT, AST, alkaline phosphatase (ALP) activities were assayed by using commercial kits (Human, Diagnostic Co. Germany), while total protein, albumin, uric acid, urea and creatinine (Crescent Diagnostic Co. KSA) were estimated spectrophotometrically (BM Co. Germany, 5010) according to enclosed pamphlets.

Cadmium and selenium measurement

The concentration of Cd in the liver was determined by atomic absorption spectrophotometry (Perkin-Elmer A.A. Model 800) with Zeeman-effect for background correction. Briefly, 0.5 g of each sample homogenized and digested with ultra-pure concentrated nitric acid: Perchloric acid at a ratio of (6:1), then complete dryness by using a hot plate. The samples were analyzed for cadmium using atomic absorption spectrophotometry after dilution with diluted with deionized water [18]. For selenium analyses, dried homogenized liver samples (0.5 g) were digested with ultra-pure nitric acid and hydrogen peroxide in the microwave digestion system. Selenium content was determined in digestion, samples by atomic absorption spectrometry [19].

Statistical analysis

Data were analyzed by means of one way (ANOVA) using the SPSS software statistical program (SPSS for windows, ver.15.00, USA) followed by least significant difference (LSD). Data are expressed as the mean ± SD, and $P < 0.05$ was considered statistically significant [20].