CADMIUM, WHICH PLAYS AN IMPORTANT ROLE IN THE DEVELOPMENT OF LUNG DISEASES, IS MOST COMMONLY ACCUMULATED IN THE LIVER

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Abstract

Cadmium (Cd) is a ductile metal in the form of a blueish or silvery-white powder. It is naturally found in soil (about 0.2 mg/kg), minerals, and water. Cd belongs to the group of toxic, carcinogenic, and stimulating elements. Some lung diseases (such as emphysema, asthma, and bronchitis) and high blood pressure are thought to be related to slow poisoning. The symptoms of cadmium poisoning may vary depending on the time of exposure, the type of diet, and the age and health status of the exposed people. For non-smokers and non-occupational exposures, the only source of exposure is diet .Its biological half-life in the human body ranges from 16 to even 30 years on average. We conducted experiments on 15 white rats weighing 140-260 g, kept in the vivarium under normal conditions at the Scientific Research Center of the Azerbaijan Medical University, and divided them into 3 groups. The concentration of lactate dehydrogenase (LDH), alkaline phosphatase (ALP), peroxidase, and catalase in the blood of white rats was determined.The results of our experiments show that cadmium poisoning increases the levels of liver enzymes and antioxidant products in blood taken from the portal vein of the liver.

Keywords: lungs, diseases, cadmium, liver

Introduction

The FAO/WHO recommends that the tolerable cadmium intake for an adult is approximately 0.4–0.5 mg/week (60–70 μg per day) [1]. Cadmium is primarily absorbed through the respiratory system (about 13–19% of Cd from the air), but it can also enter through the digestive system (about 10–44%), when dust is mixed and swallowed with saliva [2,3]. The amount of accumulated Cd ranges from 0.14 to 3.2 ppm in muscles, 1.8 ppm in bones, and 0.0052 ppm in the blood. People who are most frequently exposed to heavy metals should be continuously monitored in order to maintain a healthy lifestyle, as well as to implement effective preventive measures and improve public health [4,5].

Cadmium is mainly absorbed during inhalation, partly through the digestive system when particles of dust are swallowed with saliva . This element accumulates most often in the lungs, liver, kidneys, pancreas, testicles, muscles, adipose tissue, and skin, inhibiting the activity of sulfur-containing enzymes illustrates some of the most common sources of Cd and how Cd exposure leads to the development of lung diseases [5,7,8]. It also demonstrates the health effects associated with the long-term accumulation of Cd in the lungs. It is estimated that about 13–19% of Cd is absorbed into the lungs from the air, and about 10–44% through the digestive tract, mainly into the small intestine. Cadmium binds to red blood cells in complexes with large-molecule proteins (albumin) and accumulates in the liver, while when complexed with small-molecule proteins (metallothionein—MT) it is reabsorbed in the renal tubules [9].

The mitochondrial respiratory chain plays an essential role in maintaining energy homeostasis through oxidative phosphorylation (OXPHOS), generating energy in the form of adenosine triphosphate (ATP), which the energy necessary for life. Additionally, mitochondria are implicated in the synthesis of amino acids, lipids and phospholipids, ion homeostasis, motility, and apoptosis [10,11]. The number and functions of mitochondria differ in animal tissues and cells relative to energetic needs and in response to physiological or environmental alterations. Malfunctioning mitochondria are related to aging and many diseases, including cancer [12].

Cadmium may alter many mitochondrial proteins' activity (enzymes and transporter systems across the outer and inner membranes) by inhibiting respiratory chain enzymes , collapsing mitochondrial membrane

potential, and swelling mitochondria, causing the inhibition of respiration . Cadmium could directly increase permeability and decrease mitochondrial membrane potential, a condition that causes cytochrome C release with activation of the caspase pathway . Additionally, cadmium inhibits ATPase, lactate dehydrogenase (LDH), superoxide dismutase (SOD), and glutathione peroxidase (GPx) activities, enhancing the levels of ROS and lipid peroxidation . Cadmium seems to be involved in Fenton reactions. Even though it does not act as a catalyst in the Fenton reaction, it can produce ROS by indirectly displacing an endogenous Fenton metal (e.g., Fe^{2+}) from proteins, thus increasing the amount of free redox-active metals. Cadmium may alter the cellular redox status by reacting with exogenous and endogenous antioxidants, such as glutathione GSH . Cadmium may damage mitochondria and not only interferes with Ca^{2+} signaling but also increases mitochondrial ROS formation [4,7].

Chronic obstructive pulmonary disease (COPD) is a respiratory system disease characterized by continuous respiratory symptoms and progressive decline in lung function. There are >400 million patients with COPD worldwide, which is the third major death causes in humans. Chronic airway inflammation with massive macrophages and lymphocyte infiltration is closely associated with the progression of COPD. A great deal of studies have demonstrated that cigarette smoking is the major risk factor for the incidence of COPD. Recently, numerous studies indicate that inhalation of polluted air and atmospheric fine particles promotes the occurrence and progress of COPD. Until now, it is not clear which substances play a key role in COPD caused by polluted air and atmospheric fine particles [13,14]. .Cadmium (Cd) is a significant occupational and environmental pollutant. Occupational population are generally exposed to Cd by inhaling the polluted air in workshops. On the other side, Cd is one of the important toxic substances in atmospheric fine particles and air pollutants. The majority of people were exposed to Cd through inhaling atmospheric fine particles and air pollutants. Epidemiological research results indicated that there was an inverse correlation between occupational and environmental Cd exposure levels and lung function of the exposed population. Several hospital-based cohort studies showed that serum Cd level was affirmatively correlated with pulmonary inflammation and epithelial-mesenchymal transition (EMT) in patients with COPD [15].

The liver's main job is to filter the blood coming from the digestive tract before it circulates to the rest of the body, metabolizing and detoxifying potentially harmful chemicals and drugs. Approximately 60% of absorbed Cd is deposited in the liver (30%) and kidney (30%), while the rest is distributed throughout the other parts of the body . Approximately 0.007% to 0.009% of the Cd body burden per day is excreted through urine and feces . There are two main ways for the ionic form of Cd^{2+} to get through the hepatocyte cell membrane: (1) binding with Fe^{2+} and Zn^{2+} transporters, or (2) through voltage-gated Ca^{2+} channels . Protein-bound Cd usually binds to liver-produced metallothionein (MT) protein to form Cd metallothionein (Cd-MT) complex, which enters cells through receptor-mediated endocytosis and is then released from the Cd-MT as a Cd ion through the digestion of lysosome. Chronic Cd ion is stored in various tissues such as the liver, kidney, prostate, and bone [16]. Acute Cd poisoning causes increased levels of liver damage markers such as alanine aminotransferase (ALT), aspartate aminotransferase (AST), and alkaline phosphatase (ALP) in the blood and also increases the incidence of nonalcoholic hepatitis and fatty liver . Histopathology shows that Cd can induce acute liver injury leading to tissue necrosis, apoptosis, hyperplasia, and enlarged liver sinus and hilum . Severe necrosis is accompanied by neutrophil infiltration and chemotaxis to the lesion , which can worsen liver damage. The mechanisms of Cd-induced acute hepatic injury mainly involve two pathways . Firstly, Cd directly binds to sulfhydryl groups on key molecules including glutathione (GSH) and sulfhydryl groups of proteins to cause oxidative damage . Secondly, although Cd is not a redox-reactive metal, it can cause inflammatory injury , an event associated with oxidative stress [17].

Material and methods

Research We conducted experiments on 15 white rats weighing 140-260 g, kept in the vivarium under normal conditions at the Scientific Research Center of the Azerbaijan Medical University, and divided them into 3 groups.

While conducting experiments, the rules of behavior with experimental animals of the European Bioethical Commission (Strasbourg 1986) and the local bioethical commission of the Azerbaijan Medical University were strictly followed. n all cases, the experiments were performed under anesthesia conditions, and at the end of the experiment, anesthesia was created by injecting 0.5 ml of calypsol solution into their abdominal cavity. The white rats selected for the experiment were divided into 3 groups with 5 heads in each.

Group 1 included intact rats.

Creation of a pathological model in rats as a result of cadmium poisoning in group 2.

10 days after the cessation of poisoning, liver enzymes and a representative of the antioxidant defense system were determined in the blood of white rats in group 3.

The concentration of lactate dehydrogenase (LDH), alkaline phosphatase (ALP), peroxidase, and catalase in the blood of white rats was determined.

Results and discussion.

The results of the analyses determined that the average concentration of the LDH enzyme in the blood of intact white rats as a result of cadmium poisoning was 368±28.53 u/l (σ=63.80), and the average concentration of the alkaline phosphatase enzyme was 234±27.13 u/l (σ=60.66).

In group 2, the average concentration of LDH increased by 2% to 379±7.48 u/l (σ=16.73), and the average concentration of alkaline phosphatase increased by 2% to 271.2±23.74 u/l. The average concentration of peroxidase was (11.7±0.48 nmol/mg; σ=1.08), and the increase in its concentration compared to the intact state was 4%.

Unlike peroxidase, the concentration of catalase increased very slightly. Its average concentration was

250.6±9.27 mkat/l (σ=20.72). This was only 1% increase, much less than the level in the intact state.

Compared to group 3, the average concentration of the LDH enzyme increased by 22.5% ($p<0.05$), and the average concentration of the alkaline phosphatase enzyme increased by 9% ($p>0.05$). Thus, compared to group 2, the average concentration of peroxidase in the liver tissue of white rats included in group 3 increased by 2% and the average concentration of catalase increased by 4%. Thus, among the markers we studied, the largest increase was recorded in catalase.

The concentration of catalase in the liver tissue of white rats included in group 3 varied between 130-275 Mkat/l. Its average concentration increased sharply and reached 172±18.61 Mkat/l. The reason for this was that the concentration of catalase in the liver tissue of the white rats (10%) taken into the experiment increased to a higher level than normal.

In this regard, the average concentration of catalase in the liver homogenate was 18% ($P<0.05$) higher than the level in group 2 animals and 12% higher than the level in intact experimental animals.

Conclusions

The results of our experiments show that cadmium poisoning increases the levels of liver enzymes and antioxidant products in blood taken from the portal vein of the liver.

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