CHARPTER I

INTRODUCTION

In Mae-Sot District, Tak Province, the paddy fields receiving irrigation from the creeks before reaching the zinc area, became much higher passing through this area and then reduced according to the distance. Rice grain and soybean grown in the areas were also detected to have elevated cadmium content compared with the normal values. Since the major of residents consumed rice grown locally, they were at risk of chronic cadmium toxicity. Health risk assessment among these exposed people was launched. The major route of cadmium exposure for the general population is via food. An increase in soil cadmium content generally results in an increase of plant uptake of cadmium although some soil and plant factors may influence cadmium accumulation by plants. Crops grown in cadmium-contaminated areas have been found to contain elevated cadmium content. Therefore, human cadmium exposure via food in contaminated areas can be many times above normal intakes and lead to cadmium toxicity.

Cadmium is a toxic transition metal of occupational and environmental concern. Cadmium exposure leads to a variety of damageable effects. The biological half life of cadmium, more than 15 years, essentially makes it a cumulative toxin, so long past exposures could still result in direct toxic effects of the residual metal. Cadmium accumulates primarily in the liver and kidney where the metal is bound with metallothionein (MT) and it is shown that cadmium bound to MT is essentially de-toxicated, at least temporarily, through this high affinity sequestration. Cadmium accumulates gradually in the human body, where it gives rise to a number of adverse health effects and especially to nephrotoxicity and osteotoxicity (WHO, 1992; Nordberg, 1992). A slow combined toxic effect of cadmium in the form of osteomalacia and kidney damage in which osteomalacia and osteoporosis are secondary to renal dysfunction was first noted in Japan in the late 1940s (Kjellstrom, 1992). Itai-itai disease is considered to be the most severe form of chronic cadmium intoxication (WHO, 1992; Nordberg, 1992; Kjellstrom, 1992; Nogawa, 1981).

The clinical features of this disease include bone and kidney damage (Nordberg, 1992). Pathological bone findings are a combination of osteomalacia and osteoporosis. (Kjellstrom, 1986) In long-term exposure, the critical organ is the kidney. Renal effects have long been recognized under occupational exposure and in populations with extremely high exposure through foods. Moreover, minor effects of kidney have been reported in populations living nearby cadmium-emitting industries. The body has limited capacity to respond to cadmium exposure, as the metal is not metabolized to less toxic species and is less excreted, causing accumulate in body. There are several sources of human exposure to cadmium, including working in metal industries, battery industry, electroplating industries and smoking. Smoking is high risk exposure persons. Environmental exposure to cadmium is also not uncommon (Bertin, G., et al., 2006; Nilsson, U., et al., 2000).

Human excessive cadmium exposure via food in contaminated areas can therefore be many times above normal intakes and long-term oral exposure may lead to cadmium toxicity. Urinary excretion of cadmium is a good indicator of excessive cadmium exposure and body burden. Several studies have shown that the kidney is the main target organ for chronic cadmium exposure. The nephrotoxic effects are characterized by tubular dysfunction and tubular cell damage. An early sign of tubular dysfunction is demonstrated by increased urinary excretion of low molecular weight proteins. The renal effects of cadmium causing proteinuria may progress and lead to increased blood creatinine, decreased glomerular filtration rate (GFR), and end-stage renal disease (Ryumon, H., et al., 2010).

Urine Cd (U-Cd) concentration is influenced by the body burden, and U-Cd is proportional to the concentration in the kidneys. In general, nonsmokers have U-Cd concentrations of 0.02-0.7 μg/g creatinine, and their cadmium levels slowly increase with age in parallel with the accumulation of cadmium in the kidney. Some examples of U-Cd concentrations in the Swedish smokers and people living in contaminated areas have higher values. Smokers have concentrations that are about twice as high as nonsmokers. Measurements of U-Cd in non-occupationally exposed nonsmokers living in urban areas of Sweden showed higher concentrations in women than in men. This finding may partly be due to differences in the urinary excretion of creatinine, it being about 1.8 g/day for men and 1.2 g/day for women. There is a close

relationship between the cadmium concentrations in urine and kidneys. If one assumes a linear relationship between cadmium in urine and kidneys, which, however, may not always be totally correct, a U-Cd of 5 μg/g creatinine corresponds to a concentration of about 100 mg/kg in the kidneys, while 2.5 μg/g creatinine in urine corresponds to about 50 mg/kg in the kidneys. However, soon after an incident of high exposure to cadmium, for example, after unintentional exposure to cadmium fumes, the urinary excretion of cadmium may temporarily increase substantially without reflecting an increase in body burden. During long-term occupational exposure, the U-Cd concentration increases slowly and in proportion to the accumulated amount in the body. In cases of tubular kidney damage, the normal reabsorption of Cd-MT decreases, and the U-Cd increases. Thus, paradoxically, when the cadmium accumulation damages the kidney, the excretion of cadmium increases, and the cadmium concentration in the kidneys gradually decreases. In the long run, the concentrations of cadmium in both the kidney and urine decrease, while the tubular damage remains. (Lars Jarup, et al., 1998)

ROS can be generated by both exogenous and endogenous sources. Cadmium is one of the exogenous sources shown to indirectly produce ROS. The production and accumulation of ROS inhibit the electron transport chain in mitochondria. In general, the accumulated ROS consists of various amounts of hydrogen peroxide, hydroxyl ions, singlet oxygen, superoxide anions, lipid hydroperoxides, phospholipid hydroperoxides etc. Excessive production of ROS disturbs the balance between the ROS and antioxidant agents (enzymes and antioxidant substances) in the cells. Hydrogen peroxide is the common substrate for catalase and Glutathione peroxidase (GPx) enzymes in the cells. While catalase decomposes H_2O_2 into water and oxygen, GPx oxidizes Glutathione (GSH) to oxidized glutathione disulphide (GSSG) by utilizing H_2O_2. Another enzyme that is required for the antioxidant defense mechanism is glutathione reductase (GR). It reduces GSSG into GSH. Both GPx and GR work in tandem in the cells in order to maintain the GSH/GSSG ratio at a steady state level. When the cells are under oxidative stress, catalase, GR and GPx respond by altering their activities. (Lekan, M., Latinwo, et al., 2006)

Objectives of the study

1. To evaluate the prevalence of the cadmium-exposure individuals in Mae-Sot district, Tak province

2. Try to evaluate the metabolic status and renal function of the high cadmium-exposure individuals

3. To compare those metabolic and renal function markers between high cadmium-exposure with non-exposure or normal

4. To analyze the markers in these cadmium-exposure individuals

Expected outputs of the study

1. To identify the prevalence of the high cadmium exposure in the Mae-Sot resident in Mae-Sot district, Tak province

2. To know about the metabolic status and renal function of the high cadmium exposure population

3. To know about comparison those metabolic and renal function markers between high cadmium-exposure with normal

4. To know about the association of those markers with the oxidative stress markers in these population

Expected outcomes

1. Try to improved the health status of the Mae-Sot residents and avoid the increasing cadmium-exposure

2. In the further study in the future may try to chelate the circulating cadmium by any natural agent to improve the toxic effect and oxidative stress