A study of assessment of environmental exposure to Cadmium as a risk factor of osteoporosis

Thesis

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By

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Introduction

Cadmium is identified as a new class of endocrine disruptors, poses a threat to human health because of its long retention (decades) in the kidneys **(Aoshima et al., 2003).**

Cadmium (Cd^{2+}) is a widespread environmental pollutant present in food (mainly cereals, vegetables, & shellfish) & tobacco**.** Because tobacco smoke is a source of Cadmium contamination, the Bone skeleton of smoker females (pre & post-menopausal) & males are generally considered to be at increased risk of exposure to toxic levels of Cadmium, not only smokers but also welders, battery factories workers and smelters are exposed to toxic levels of Cadmium **(Mussalo-Rauhamaa et al., 1986).**

Cadmium has a long biological half-life of 15-30 years mainly due to its low rate of excretion from the body, and accumulates over time in blood, kidney, and liver. Long-term exposure to cadmium may cause kidney and bone damage the most well-known example is the itai-itai disease in Japan. So there relationship between tubular damage and osteoporosis as urinary cadmium used as the dose estimate for cadmium **(Henson and Anderson, 2000).**

Cigarette smoking while being an important source of cadmium intake is also independently associated with bone loss and thus is a significant confounder of the relationship between cadmium exposure and bone loss. Osteoporosis may be estimated objectively by measurement of bone mineral density (BMD), Dual x-ray Absorptiometry (DXA) **(Honda et al., 2003).**

Osteoporosis is a common metabolic disease characterized by low bone mass & microarchitectural deterioration of bone tissue, it is a major cause of morbidity worldwide **(Alfven et al., 2000).**

Women who smoke one pack of cigarettes each day throughout adulthood will, by the time of menopause, have an average deficit of 5 to 10 percent in bone density, which is sufficient to increase the risk of fracture **(Riggs et al., 2005).**

Cadmium induced reduction in the Hydroxylaion of 25-HCC to the active form 1,25 DHHCC occurs following renal tubular damage by cadmium. The decreased activation of vitamin D due to cadmium induced renal tubular damage has been considered to be crucial for the induction of bone effects of cadmium (**Buchet et al., 1995).**

Cadmium may also act directly on bone. An in vitro study of culture of a clonal osteogenic cell showed that the mineralization of the cells was significantly decreased following the additional of Cadmium ions together with a decrease in collagen content and alkaline phosphatase activity. This indicates that Cadmium may interfere directly with the mineralization of bone cells **(Miyahara et al., 1990).**

Animal studies have shown Cadmium to stimulate the formation activity of osteoclasts, breaking down the collagen matrix in bone to release calcium into blood **(Bhattacharyya et al., 1988).**

Epidemiological studies provided equivocal results concerning the effects of lead and cadmium on Bone density **(Bhattacharyya et al., 1988).**

Aim of the Work

Aim of this work is to study the relation of environmental exposure of Cadmium & osteoporosis in male smokers.

Cadmium, Lead and Their Effects on Human Health

Heavy Metals:

A heavy metal is any of a number of high atomic weight elements, which have the properties of a metallic substance at room temperature. There are several different definitions concerning which elements fall in this class designation. According to one definition, heavy metals are a group of elements between copper and bismuth on the periodic table of elements having specific gravities greater than 4 ***(Kuhn, 2004).***

Heavy metal toxicity:

Heavy metal toxicity represents an uncommon, yet clinically significant medical condition, if unrecognized or inappropriately treated, heavy metal toxicity can result in significant morbidity and

mortality. The periodic table contain 105 elements, of which 80 are considered metals: Toxic effects in humans have been described for less than 30 of these. Many metals are essential to biochemical processes, and others have found therapeutic uses in medicine. Iatrogenic metal toxicity may occur with bismuth, gold, gallium, lithium and aluminum, species. Intentional or unintentional ingestion of arsenic has been notions as a means of suicide and homicide ***(Diffus, 2004)***.

However, occupational exposure to heavy metals has accounted for the vast majority of poisoning throughout human history. Toxic effects of chronic exposure to heavy metals are far more common than acute poisoning. Chronic exposure can lead to variety of conditions depending on route of exposure, and the metabolism and storage of the specific element in question ***(Baselt, 2000).***

For example, chronic exposure to cobalt dust has been associated with the development of pulmonary fibrosis that can lead to core-pulmonale. This hard

metal pneumoconiosis has been described for other metal dusts. Chronic inhalation of high doses of cadmium also cause fibrotic and emphysematous lung damage but it also has major effects on bone and genitalia. Itali-Itali (ouch-ouch) disease, a syndrome of chronic renal failure and osteoporosis described in Japan, is often attributed to high levels of naturally occurring cadmium in the soil coupled with increased industrial exposures ***(Mench et al., 1998).***

Pathophysiology of heavy metals toxicity:

The pathophysiology of the heavy metal toxidromes remain relatively constant: For the most part, heavy metals bind to oxygen, nitrogen, and sulfhydryl groups in proteins, resulting in alterations of enzymatic activity. This affinity of metal species for sulfhydryl groups serves a protective role in heavy metal homeostasis as well. Increased synthesis of metal binding proteins in response to elevated levels of a number of metals is the body's primary defense mechanism against poisoning. For example, the

metalloproteins are induced by many metals. These molecules are rich in thiol ligands, which allow high affinity binding with cadmium, copper, silver, zinc, lead and others. Other proteins involved in both heavy metals transport and excretion through the formation of ligands are ferritin, transferring, albumin and hemoglobin ***(Cravery, 1998).***

Although ligand formation is the basis for much of the transport of heavy metals throughout the body, some metals may compete with ionized species such as calcium and zinc to move through membrane channels in the free ionic form. For example, lead follows calcium pathway in the body, hence, its deposition in bone and gingivae ***(Keating, 1997)***.

Nearly all organ systems are involved in heavy metals toxicity, however the most commonly involved organ systems include the central and peripheral nervous system, gastrointestinal tract, haemopoietic, renal and cardiovascular system. To a lesser extent, lead toxicity involves the musculoskeletal and reproductive

systems. The systems affected and the severity of the toxicity vary with the particular heavy metal involved the age of individual, and the level of toxicity ***(Keating, 1997).***

Frequency:

In the U.S: heavy metals toxicity by chronic lead exposure is the most commonly encountered. The National Health and Nutrition Examination survey (NHANES III) conducted from 1988-1999 found that 0.4% of persons aged 1 year and older have blood levels of lead of 25 mg/dL or higher. The data also noted that, among those aged 1-5 years, an estimated 1.7 million children have blood levels greater than 10 mg/dL. The syndrome of childhood plumbism caused by the ingestion of lead is believed to affect more than 2 million American pre-school aged children. Lead toxicity has a significantly higher prevalence among the African, American population and in lower socioeconomic areas. Reliable figures for the prevalence of mercury and arsenic toxicities are not