CADMIUM ACCUMULATION IN THE MAIN ORGANS DURING A CHRONIC EXPOSURE

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Key words: cadmium, chronic toxication, gonads, kidney, liver.

SYNOPSIS

In this study was made the assessment of Cd accumulation in the main organs and Cd accumulation in the reproductive system. As indicator species we used Cavia porcellus. In the groups of experiment were injected intraperitoneally CdCl₂ solution in three different doses, TDI (tolerable daily intake), intermediate dose and LD₅₀-5% for 60 days. At the end of this treatment the animals were sacrificed and the samples of blood, livers, lungs, kidneys and gonads were analyzed for Cd content in AAS and compared to those of a control group. The results showed that the liver accumulate the greatest burden of Cd followed by the kidneys.

INTRODUCTION

Increasing industrialization all over the world has been associated with the extraction and distribution of minerals from their natural deposits. Many of them have been subject to chemical changes due to technological processes and finally passed in waters, earth and air and thus the food chains. This includes heavy metals.

Some heavy metals, including cadmium, are cumulative toxins. The risk of chronic toxication is the biggest problem. Among negative effects of heavy metals in humans and animals are disorders of different enzymatic systems resulting in injured tissues and main organs including nervous system, endocrine system, lungs, liver, kidneys, reproductive organs etc. The impact of heavy metals can induce the change of certain genes the expression.
Cadmium and its compositions are poorly absorbed; only <1% of the cadmium taken in inhalator, oral or dermal route is absorbed. Different factors can affect the efficiency of oral or inhalator absorption. Absorbed cadmium is excreted too slowly with urine and feces in almost equal proportions. Nearly 0.007% and 0.009% are excreted in urine and feces respectively each day. Cadmium is distributed all over the organism with the greater portion of body burden in the liver and kidneys. Humans and animals have similar characteristics in the distribution of cadmium and this is independent to the route of exposure, but dependent to the exposure duration (Nordberg et al., 1987, Kjellstörm et al., 1978, Wester et al., 1992).

Distribution of cadmium in animals after oral exposure is similar to that in humans with the greatest accumulation in the liver and kidneys and lower accumulation in the other parts of the organism (Kotsonis & Klaassen, 1978; Weigel et al., 1984). Concentrations of cadmium in the liver and kidneys are comparable after short-term exposure (Andersen et al., 1988; Jonah & Bhattacharyya 1989), but the cadmium concentration in kidneys passes that of the liver after long-term exposure (Kotsonis & Klaassen, 1978), except very high doses of exposure (Ando et al., 1998; Bernard et al., 1980; Hiratsuka et al., 1999). In mice exposed in oral route to cadmium during lactation, 53% of the cadmium body burden was found in the kidneys, compared with 27% in control non pregnant animals (Bhattacharrya et al., 1982).

Cadmium in the milk is 5-10% of its level in the blood. This may be because of inhibition of transfer from the blood to milk as cadmium get linked in the blood cells by metalotionine (Radisch et al., 1987).

The half-life of cadmium in human organism is >26 years (Shaikh & Smith, 1980) and few months to few years in mice, rabbit and monkeys (Kjellström & Nordberg, 1978).

Chronic exposure to cadmium causes lesions of the proximal tubules, proteinuria (β2-microglobulin), glicosuria, aminoaciduria, poliuria, reduction of phosphate absorption and enzymuria in humans and laboratory animals. Clinical sings result from degeneration and atrophy of proximal tubules or interstitial fibrosis of the kidneys (Stowe et al., 1972). It has been proved that cadmium affects lipid content and stimulate their peroxidation (Gill et al., 1989b). Cadmium alters zinc, iron and copper metabolism (Petering et al., 1979) and also selenium metabolism (Jamall & Smith, 1985; Xu et al., 1995) proposed that an initial step of cadmium induced toxicity in testis is the intervention of cadmium in complexes zinc-protein that control the DNA transcription, which leads to apoptosis. Acute or chronic doses of cadmium reduce hepatic glycogen reserves and increase glucose blood levels.

It is possible that cadmium act directly or indirectly in reduction of the bones mineral density, increasing the possibility of fractures (Brzóska & Moniuszko-Jakoniuk, 2005a, 2005b). Studies in small animals suggest that cadmium inhibits
osteoblastic activity resulting in reduction of organic matrix synthesis and mineral content of the bones (Brzóska & Moniuszko-Jakoniuk, 2005d).

**SUBJECT AND METHODS**

The purpose of this study was the evaluation of the map cadmium distribution in the main organs to highlight the place of reproductive organs in this map. In this study were used 80 animals, sexually mature Guinea pigs (*Cavia porcellus*) (body weight 400-600 g). The animals were divided into two big groups with 30 individuals each (30 female, 30 male) and a control group of 20 individuals (10 females and 10 males).

Administration of the metal was made in three different doses, TDI (tolerably daily intake), LD_{50*5}*5% (to avoid the death till the end of the experiment) and an intermediate dose. The doses were injected intraperitoneally (in the lower abdominal quadrant) in form of CdCl₂ aqueous solution. In this route the volume injected can reach 10-15 ml for adult guinea pigs (Beynon & Cooper, 1991). The doses applied were TDI 0,0005 mg Cd/kgbw/day (RIVM report 711701 025, 2001), LD₅₀*5% 0.2177 mg Cd/kgbw/day and the intermediate dose 0.1148 mg Cd/kgbw/day.

Blood samples were collected every week via cardiac puncture (Beynon & Cooper, 1991). After 60 days of experimentation the animals were sacrificed and during their dissection the main organs were extracted; liver, kidney and lungs. Testis and ovaries were also extracted. All the samples were analyzed for cadmium content with the technique of Atomic Absorption Spectrometry (AAS). The spectrometer used was type Varian, Spectr-200 with limit of detection for cadmium 0,006 ppb (µg/L). These examinations were made at the laboratory of Analytic Chemistry, Institute of Food Safety and Veterinary, Tirana, Albania.

**RESULTS AND DISCUSSIONS**

Data obtained from the examination of all samples for cadmium content were transformed in mean values and then organized in tables to evaluate accumulation and distribution of cadmium in organism (referring to the main organs) depending on the dose used. These tables were used to compare distribution of cadmium in males and females and also in different doses applied. The tables are graphically illustrated to visualize the levels of cadmium accumulation and its distribution in the organs according to different doses applied in the two sexes. Zero values are actually values below the limit of detection of apparatus used.

In tables 1 and 2 is presented the accumulation of cadmium in liver, kidney, lungs, gonads and blood grouped according to the doses applied.
Table 1: Cd accumulation in the main organs in males (ppm).

<table>
<thead>
<tr>
<th>Organ</th>
<th>liver</th>
<th>kidney</th>
<th>lung</th>
<th>testes</th>
<th>blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>0.178</td>
<td>0.276</td>
<td>0.051</td>
<td>0.092</td>
<td>0.001</td>
</tr>
<tr>
<td>TDI</td>
<td>0.166</td>
<td>0.690</td>
<td>0.004</td>
<td>0.961</td>
<td>0.000</td>
</tr>
<tr>
<td>Int.dose</td>
<td>118.170</td>
<td>40.242</td>
<td>1.490</td>
<td>3.474</td>
<td>0.231</td>
</tr>
<tr>
<td>LD₅₀-5%</td>
<td>222.273</td>
<td>87.609</td>
<td>8.091</td>
<td>9.313</td>
<td>0.494</td>
</tr>
</tbody>
</table>

Table 2: Cd accumulation in the main organs in females (ppm).

<table>
<thead>
<tr>
<th>Organ</th>
<th>liver</th>
<th>kidney</th>
<th>lung</th>
<th>ovary</th>
<th>blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dose</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Control</td>
<td>0.158</td>
<td>0.623</td>
<td>0.076</td>
<td>0.176</td>
<td>0.000</td>
</tr>
<tr>
<td>TDI</td>
<td>0.230</td>
<td>0.852</td>
<td>0.021</td>
<td>0.877</td>
<td>0.003</td>
</tr>
<tr>
<td>Int.dose</td>
<td>112.520</td>
<td>36.336</td>
<td>2.944</td>
<td>13.716</td>
<td>0.135</td>
</tr>
<tr>
<td>LD₅₀-5%</td>
<td>194.304</td>
<td>76.200</td>
<td>4.370</td>
<td>44.817</td>
<td>0.356</td>
</tr>
</tbody>
</table>

According to these results, is observed a great cadmium concentration in the liver, kidneys and ovary, and a lower concentration in lungs, testes and blood. In absolute values, the greatest cadmium concentration is reached in the liver of the groups treated with LD₅₀-5% dose; 222.273 ppm in males and 194.304 ppm in females. So, from all the organs examined, the liver contains the greater burden of the cadmium. Cadmium concentration in blood increases in parallel with increasing of doses, but it always stays in low levels, confirming once again the role of blood as a transporter for the toxin in question (Kotsonis & Klaassen, 1978; Weigel et al., 1984).

Table 3 presents the relative distribution of cadmium in main organs and blood (relative to cadmium levels in the liver) in the groups of males according to the doses applied and table 4 presents the relative distribution of cadmium in females.

Table 3: Relative distribution of Cd in organs in males.

<table>
<thead>
<tr>
<th>Organ Dose</th>
<th>liver</th>
<th>kidney</th>
<th>lung</th>
<th>testes</th>
<th>blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>1.000</td>
<td>1.551</td>
<td>0.287</td>
<td>0.517</td>
<td>0.006</td>
</tr>
<tr>
<td>TDI</td>
<td>1.000</td>
<td>4.157</td>
<td>0.024</td>
<td>5.790</td>
<td>0.000</td>
</tr>
<tr>
<td>Int.dose</td>
<td>1.000</td>
<td>0.341</td>
<td>0.013</td>
<td>0.029</td>
<td>0.002</td>
</tr>
<tr>
<td>LD₅₀-5%</td>
<td>1.000</td>
<td>0.394</td>
<td>0.036</td>
<td>0.042</td>
<td>0.002</td>
</tr>
</tbody>
</table>
Table 4: Relative distribution of Cd in organs in females.

<table>
<thead>
<tr>
<th>Dose</th>
<th>liver</th>
<th>kidney</th>
<th>lung</th>
<th>ovary</th>
<th>blood</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td>1.000</td>
<td>3.954</td>
<td>0.480</td>
<td>1.117</td>
<td>0.000</td>
</tr>
<tr>
<td>TDI</td>
<td>1.000</td>
<td>3.704</td>
<td>0.091</td>
<td>3.813</td>
<td>0.011</td>
</tr>
<tr>
<td>Int.dose</td>
<td>1.000</td>
<td>0.323</td>
<td>0.026</td>
<td>0.122</td>
<td>0.001</td>
</tr>
<tr>
<td>LD$_{50}$-5%</td>
<td>1.000</td>
<td>0.392</td>
<td>0.022</td>
<td>0.231</td>
<td>0.002</td>
</tr>
</tbody>
</table>

The relative distribution of cadmium in kidneys in control and TDI groups (males and females) is greater than 1, this means that the concentration of cadmium in kidneys is greater of that in the liver. In intermediate and LD$_{50}$-5% doses this value is lower than 1. Also in gonads with increasing of the dose applied, from TDI to LD$_{50}$-5% dose, the relative concentration of cadmium decreases.

Figure 1 and figure 2 illustrate cadmium distribution in examined organs and tissues in percentage, grouped according to sex and doses applied.

In control groups, most of the cadmium is accumulated in kidneys and bound to proteins of low molecular weight (mainly renal metalotionine). Cadmium
accumulated in the liver is several times lower than in kidneys, and lungs contain a relatively small amount of cadmium. Cadmium level in ovaries and testes is similar, 17% and 15% respectively.

In groups treated with TDI dose (figures 3 and 4) resulted a great increase of cadmium concentration in testes and ovaries compared to control group, reaching values of 53% in testes and 44% in ovaries. Cadmium levels are lower in the liver and kidneys of these groups. Lungs and blood remains in very low levels of cadmium content compared to other organs examined.
In groups treated with intermediate dose (figures 5 and 6) the level of the cadmium increase drastically reaching values of 72% and 68%. The cadmium burden in kidney and gonads decrease.

In groups treated with LD$_{50}$-5% dose (figures 7 and 8), resulted nearly the same tableau, as for the intermediate dose, for all the organs and tissues examined for cadmium content. Cadmium levels in ovaries of animals treated with intermediate and LD$_{50}$-5% doses are greater than those of testis from animals treated with the same doses.
The decrease of cadmium levels in kidneys from groups of animals treated with high doses is a consequence of severe renal injuries, one of primary toxic effects of cadmium. Renal injuries cause excretion of an amount of cadmium bound to proteins (consequence of severe injuries to proximal tubules cells) (Andersen et al., 1988; Jonah & Bhattacharyya, 1989; Kotsonis & Klaassen, 1978; Mason, 1990).

The histograms below present cadmium concentration in ppm reported in tables 1 and 2 grouped according to sex and organs with comparable cadmium levels.

![Figure 9: Cd accumulation in liver and kidneys in males.](image)

![Figure 10: Cd accumulation in liver and kidneys in females.](image)

In males (figure 9) as in females (figure 10) the dynamic of cadmium accumulation is the same. Cadmium concentration in the liver is greater than that in the kidneys.
The dynamic of cadmium accumulation in lungs and blood is the same, but there is a considerable difference in cadmium concentration values (figures 11 and 12).
Cadmium accumulation in gonads, illustrated in figure 13, shows a proportional increase of cadmium concentration in testes and ovaries with the increase of the dose applied. Cadmium accumulation in ovaries is several times greater than cadmium accumulation in testes.

CONCLUSIONS

- In low cadmium doses applied, kidneys contain a great portion of cadmium body burden, followed by the liver; increasing of cadmium dose leads to increased cadmium burden in the liver passing that of the kidney.
- Cadmium circulating with the blood constitute a small portion of cadmium body burden, serving mainly as a transporter to other organs
- Cadmium accumulation in other organs or tissues is similar in males and females.
- Cadmium accumulation for the same doses applied, is greater in ovaries than in testes.

REFERENCES:


Jonah, M.M., Bhattacharyya, M.H. 1989: Early changes in the tissue distribution of cadmium after oral but not intravenous cadmium exposure. - Toxicology, 58:325-338.


