Effect of Chronic Exposure of Cadmium Chloride in Drinking Water on Structural and Functional Aspects of Thyroid Gland in Mature Male Rabbits*1

Samir H. Cheyad*,1, Kalisa K. Khudier**, and Khtan A. AL-Mzain**

* Ministry of Industry, General Commission for Industrial Research and Development AL-Razi Center for Research and Medical Diagnostics.
** Department of Physiology, College of Veterinary Medicine, University of Baghdad, Baghdad, Iraq.

Abstract

The effect of chronic exposure to two different levels of cadmium chloride (CdCl₂) 30 ppb and 40 ppb in drinking water for 12 weeks on thyroid function of mature male rabbits was studied. Eighteen mature male rabbits were randomly divided into three groups (each of six), control group (group I): were offered ordinary tap water, and treated groups (II and III) were offered tap water containing 30 ppb and 40 ppb respectively for 12 weeks. Serum concentration of thyroxin (T₄) and triiodothyronine (T₃) were measured every six weeks, as an index of thyroid function, further, section of thyroid gland were prepared for histological studies. The results showed that chronic exposure of male rabbits to two different levels of CdCl₂ caused significant decrease (p<0.05) in serum T3 and T4 in both treated groups in compared with control group, in addition, there were histological changes in thyroid gland of treated groups manifested by hyperplasia with presence of large number of varying size of microfollicels and hypertrophic thyrocytes, small colloid with little secretion.

Key wards: Cadmium, Thyroid gland, Thyroxin, Triiodothyronin, Thyrocyt

Introduction

Cadmium is modern toxic metals (discovered in 1817). Its main use in electroplating because of its anticorrosive properties, it also used as color pigment of paints, plastics and as cathode material for nickel –cadmium batteries, cadmium is an important source of environment pollution (1). Hazardous waste disposal sites are large source of Cd concentration found in soil and water. Tobacco smoke is the main reason for cadmium accumulation in our body (2), on other hand, the major route of cadmium intake (for non smoker) is ingestion, this is largely due to the presence of Cd (2-40 ppb) in food staff of natural origin e.g. cereals beans, carrots, beverage, coffee and tea (3), or by the ingestion of contaminated food especially fish (4, 5). The acute toxic effect of Cd are generally restricted to the lung where as the effects following chronic Cd exposure in human are multisystemic and include nephropathies emphysematous alteration in the lung, cardiovascular disease, and bone damage possibly (osteomalacia and osteoperosis) (6). Wealth of evidence suggested that heavy metals including cadmium exert profound toxic effects on the activities of a number of endocrine gland including thyroid gland (7, 8).

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1Corresponding author E-mail : samir-cheyad@yahoo.com
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Cadmium intoxication has been reported to reduce the thyroid iodide uptake (7) and inhibits hepatic conversion of thyroxin (T4) to triiodothyronine (T3) in rats (9) and mice (10). It has been previously reported that subcutaneous injection of cadmium chloride (CdCl2) (mg/kg B.W) for ten weeks to male rabbits resulted in a significant reduction in serum T3 concentration and hepatic T4 production (11). The direct relationship between heavy metals poisoning and thyroid dysfunction were studied in male rabbits by Ghosh and Battacharya,1992. within 24 hours of intramuscular injection of CdCl2 (15mg/kg B.W) a significant increase in thyroid activity over the control with a concomitant rise in T3 titer were observed. The toxic effect of cadmium on thyroid gland functions has been studied, yet its effect at above the permissible level and below the toxic one are questioned, to this aim the present study dedicated.

Materials and Methods

Number of mature male rabbits 800-1000 g of local breed were acclimated to holding facilities for one week prior to commencement of dosing. Animals in all stages of experiment were housed in clear plastic cages in conditioned room (22-25 c°) with controlled lightening, eighteen rabbits were randomly and equally divided into three groups and were treated for three months as follow : group I, rabbits in this group were received tap water and served as a control, group II were received 30 ppb of cadmium chloride in drinking water, while the figure 3 showed a large area of hyperplasia manifested by presence of thyroid microfollicels of varying size lined by hyperphtoic thyrocyte , small colloid with little secretion in follicular lumen ( figure 2), while the figure 3 showed a large area of irregular and varying size microfollicels with hyperphtoic thyrocyte with little colloid secretion.

Table 1: Serum triiodothyronine (T3) concentration (nmol/l) in rabbits treated with two different levels of cadmium chloride in drinking water.

<table>
<thead>
<tr>
<th>Time (weeks)</th>
<th>Groups</th>
<th>I</th>
<th>II</th>
<th>III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-treatment</td>
<td>0</td>
<td>0.43±0.01 A a</td>
<td>0.44±0.01 A a</td>
<td>0.44±0.01 A a</td>
</tr>
<tr>
<td>During treatment</td>
<td>6</td>
<td>0.45±0.01 A a</td>
<td>0.43±0.01 A a</td>
<td>0.41±0.02 B b</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>0.44±0.01 A a</td>
<td>0.40±0.02 B b</td>
<td>0.40±0.02 B b</td>
</tr>
</tbody>
</table>

Values are expressed as mean ±SE n = 6/group Groups: I = control, II = rabbits received 30 ppb of cadmium chloride in drinking water, III = rabbits received 40 ppb of cadmium chloride in drinking water. Capital letters denote between group differences, P< 0.05 vs. control. Small letters denote within same group differences, P<0.05 vs. pretreated values.

Results

The effect of the two different levels of cadmium chloride on mean values of serum T3 concentration of male rabbits are shown in table (1), serum T3 concentration showed a significant decrease (p<0.05) at the 6th week of exposure to cadmium chloride in group III and at the 12th week of experiment in group II as compared with control. In cadmium treated groups. In table(2) thyroin serum concentration significantly decreased (p<0.05) compared to control , such decrement was observed at the 6th–12th week of experiment. Within groups, the values tended to decrease significantly (p<0.05) with time (at 6th–12th week) as compared with the pretreated period. The histological structure of thyroid gland of un treated rabbits was shown in figure (1), the thyroid follicles containing colloid of uniform color, oval in shape, lined by cuboidal thyroid follicular cells, figures 2,3 illustrated the histological changes in thyroid gland of rabbits following 30 and 40 ppb of CdCl2 (group II and group III), the figures showed a case of hyperplasia manifested by presence of thyroid microfollicels of varying size lined by high columnar thyroidal follicular cells (hypertrophic thyrocyte), small colloid with little secretion in follicular lumen (figure 2), while the figures showed a large area of irregular and varying size microfollicels with hypertrophic thyrocyte with little colloid secretion.
Table 2: Serum tetraiodothyronine (T4) concentration (nmol/l) in rabbits treated with two different levels of cadmium chloride in drinking water.

<table>
<thead>
<tr>
<th>Time (weeks)</th>
<th>Groups</th>
<th>I</th>
<th>II</th>
<th>III</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pre-treatment</td>
<td>0</td>
<td>58.17±0.7 A a</td>
<td>57.42±0.56 A a</td>
<td>57.12±0.42 A a</td>
</tr>
<tr>
<td>During treatment</td>
<td>6</td>
<td>58.5±1.25 A a</td>
<td>51.0±2.4 B b</td>
<td>49.2±1.6 B b</td>
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<tr>
<td></td>
<td>12</td>
<td>58.35±1.3 A a</td>
<td>44.5±1.9 B c</td>
<td>41.7±0.4 B c</td>
</tr>
</tbody>
</table>

Values are expressed as mean ± SE. n = 6/group.

Groups:
- I = control
- II = rabbits received 30 ppb of cadmium chloride in drinking water
- III = rabbits received 40 ppb of cadmium chloride in drinking water

Capital letters denote between group differences, P<0.05 vs. control.
Small letters denote within group differences, P<0.05 vs. pretreated values.

Discussion
This study showed that exposure of rabbits to cadmium brings the animal to the case of hypothyroidism manifested by significant decrease in serum T3 and T4 concentration associated with biological changes. To the best of our knowledge, the effects of chronic exposure to CdCl2 at levels 30 and 40 times above the permissive level on thyroid gland feature have not been studied yet, however considerable body of evidence how exist attesting the involvement at heavy metals including cadmium in the toxicity of a number of endocrine glands including thyroid gland (8,9). Many studies suggested the mechanisms including affecting hepatic thyroxin metabolism through reduction in the activity of hepatic “Outer Ring Deiodinase ORD” an
enzyme which responsible for conversion of major circulating form of thyroid hormone (T4) to more biologically active form(T3) with disruption of T3 signaling leading to reduction in T4 conversion (15). In addition cadmium may cause reduction of thyroidal I uptake by damages the structure and function of both follicular and parafollicular cells of thyroid (9,10). Long term exposure to cadmium may induce the activity of hepatic microsomal enzyme especially UDP-GT (Uridine DiPhosphate Glcucourynl Tranferase ) (16) and phenol sulfttransferase (17) resulting in rapid clearance of T3 and T4 , on other hand , accumulation of cadmium in mitochondria of thyroid follicular epithelial cells might disturb the oxidative phosphorylation of this organelle with subsequent loss of energy supply leading to inhibition in the synthesis and release of thyroid hormone (18). The suspected selenium deficiency caused by cadmium treatment may lead to histological changes by activation fibrotic process in which inflammatory reaction and excess transforming growth factor B play a role in thyroid gland morphology . (19) Gupta P and Kar A (1999) study the relation between cadmium and selenium , vitamin E and thyroid dysfunction in chicken, in this study they suggested that cadmium decrease T3, probably by inhibiting hepatic 5-monodeiodinase (5D-I)activity, which is a selenium dependent function. Cadmium is known selenium antagonist while vitamin E facilitate selenium metabolism . Vitamin E was shown to protect against cadmium toxicity and maintain 5D-I activity and T3 levels, while the experimenters concluded that the metal – induced inhibition in hepatic 5 D-I activity is mediated through lipid piroxidation my conclusion is that the cadmium inhibited 5D-I activity by decreasing selenium. While vitamin E does decrease lipid piroxidation it does this by facilitating selenium metabolism and selenium is the key metal in glutathione peroxidase which is a potent inhibitor of lipid piroxidation (9) Accordingly we can speculate that selenium deficiency may occur in this study following cadmium exposure resulting in the damage of thyroid gland , decrease the concentration of both (T3 and T4) and inhibit monodeiodinase activity leading to state of hypothyroidism .

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References
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