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Effects of lead on thyroid functions in lead-exposed workers

Research Article

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Abstract: Lead exposure is a common public health problem. Exposure to the metal can cause hematological, gastrointestinal, rheumatological, endocrine, neurological and renal problems in humans. However, effects on the thyroid gland are controversial. We retrospectively investigated thyroid function parameters in 65 adult males who had been occupationally exposed to lead. We then compared the findings with those of 60 male patients who had no history of lead exposure or thyroid abnormalities, who served as the control group. The mean ages of the lead-exposed workers and the controls were 34.3 ± 7.9 and 32.9 ± 6.6 years respectively. Blood lead levels in the lead-exposed workers were significantly higher than in the control group. The lead-exposed workers were assigned to one of three groups according to their blood lead levels, as follows: 40 - 59 μg/dl, 60 - 79 μg/dl, or 80 μg/dl and above. Thyroid Stimulating Hormone (TSH) levels in the 80 μg/dl and above group were significantly higher than in either the 40 - 59 μg/dl group or the 60 - 79 μg/dl group. However, TSH levels in the 40 - 59 μg/dl group did not differ significantly from those in the 60 - 79 μg/dl group. These results suggest that high levels of lead in the blood may affect thyroid physiology. Clinicians should be aware of the potential hazardous effects of lead on the thyroid, especially in patients who have been occupationally exposed to lead.

Keywords: *Lead • Thyroid hormones • Occupational exposure*

1. Introduction

Lead is one of the most commonly used heavy metals and it has had wide applications since ancient times. However, it is also one of the most detrimental pollutants in the industrial environment in many countries. Occupational and environmental exposures to lead continue to be among the most significant public health problems [1-3]. Lead can have adverse effects on many organ systems, and various effects of lead on thyroid functions have been reported in the past 50 years [4-8]. However, findings have been inconsistent and sometimes contradictory, and no consensus has been reached regarding the effect of lead on thyroid physiology. The purpose of this study was to investigate the potential effects of lead on thyroid functions by comparing thyroid parameters in lead-exposed workers to those in healthy controls.

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Table 1. Measured parameters of the lead-exposed and control patients.

Groups	Number of patients	Mean age (years)	Mean blood lead levels (μg/dl)	Mean lead exposure time (months)	sTSH (μIU/mL)	fT3 (pg/mL)	fT4 (ng/dl)
Lead-exposed	65	34,3 ± 7,9	71,1 ± 22,8	79 ± 74	4,3 ± 2,7	2,9 ± 0,4	1,4 ± 1,1
Control	60	32,9 ± 6,6	0,2 ± 0,2	0,0 ± 0,0	1,6 ± 0,7	2,8 ± 0,6	1,1 ± 0,3

2. Material and Methods

2.1. Participants

In this study, we retrospectively examined the records of 65 men who had been exposed to lead while working as automotive mechanics or in battery factories. According to the Turkish labor rules, all workers have to undergo a complete health examination before the onset of their job position. Also, if they are working with hazardous materials, they must undergo periodic health examinations at occupational disease clinics or hospitals. Therefore, all workers were considered generally healthy before working as mechanics or battery workers. There were no thyroid diseases apparent in their medical history. Their physical examination records showed no thyroid abnormalities. All were have normal thyroid function test results. The study group participants continued to work for same factory positions during the entire course of the study. They were all exposed to lead via inhalation of the lead vapor. As a control group, the records of 60 age-matched male patients with no history of lead exposure or thyroid abnormalities were examined.

2.2. Lead measurement

For the measurement of lead levels in blood (Pb-B), 5 ml of blood was obtained from the antecubital vein and was collected in non-heparinized lead-free tubes. Measurements were made with a UNICAM 939 atomic absorption spectrophotometer (Unicam Atomic Absorption, Cambridge, UK) using a UNICAM FS90 graphite lamp (Unicam). All measurements of samples were corrected with respect to reference solution values. Lead measurement procedures were done with the method which Yee et al. were described [9]. The results were obtained as μg/dl.

2.3. Serum thyroid hormone profile

Blood was obtained for the measurement of lead levels. Blood samples of 5 ml were collected in a separate tube for fluorescent-enzyme immunoassay (FEIA) of serum free triiodothyronine (fT3), free thyroxine (fT4) and sensitive thyroid stimulating hormone (sTSH). All measurements were done with TOSOH AIA 21 analyser (TOSOH Corporation, Tokyo, Japan) usung the TOSOH reagents. The methods described in Tietz Textbook of Clinical Chemistry were used for determination of fT3, fT4 and sTSH [10]. All measurements were duplicated to determine variations. If the variations were less than 10% between the measurements, these were accepted as valid.

2.4. Statistical analysis

The groups were investigated for significant differences with the use of the Mann- Whitney and Kruskal-Wallis tests. In all comparisons, differences were considered significant with $p < 0.05$. All statistical analyses were performed with SPSS for Windows, version 11.0.

3. Results

The mean ages of the lead-exposed workers and the control patients were 34.3 ± 7.9 and 32.9 ± 6.6 years, respectively ($p > 0.05$).

Findings for the lead-exposed and control patients are summarized in Table 1. As expected, blood lead levels in the lead-exposed workers were significantly higher than in the control group ($p < 0.05$). As a function of lead exposure time, blood lead levels did not differ significantly within the lead-exposed group when participants were grouped according to exposure times of 0-11 months, 12-59 months or 60 months and above ($p > 0.05$). Levels of fT4 differed significantly between the lead-exposed workers and the control group ($p < 0.05$). Levels of sTSH in the lead-exposed group were significantly higher than in the control group ($p < 0.05$).

The lead-exposed workers were assigned to one of three groups according to their blood lead levels, as follows: 40 - 59 μg/dl, 60 - 79 μg/dl, or 80 μg/dl and above (Table 2). TSH levels in the 80 μg/dl and above group were significantly higher than in either the 40 - 59 μg/dl group or the 60 - 79 μg/dl group. However, TSH levels in the 40 - 59 μg/dl group did not differ significantly from those in the 60 - 79 μg/dl group.

Differences in fT4 levels were significant in all pairwise comparisons of the 40 - 59 μg/dl, 60 - 79 μg/dl, and 80 μg/dl and above groups (Table 2).

Table 2. Mean values of sTSH, fT3 and fT4 levels according to blood lead subgroups.

Blood lead level (μg/dl)	Number of subjects (n)	sTSH level (μIU/mL)*	fT3 level (pg/mL)†	fT4 level (ng/mL)‡
40,01-60 (Group 1)	23	3,6±1,9	2,81±0,37	1,13±0,17
60,01-80 (Group 2)	26	3,7±2,2	2,96±0,22	1,56±0,72
80,01+ (Group 3)	16	6,2±3,7	3,12±0,46	1,43±0,18

(*): Difference between group 1 and 2 was not significant ($p > 0.05$) whereas differences either between group 2 and group 3 or between group 1 and group 3 were significant ($p < 0.05$)
(†): Differences between group 1 and group 2, and group 1 and group 3 were significant ($p < 0.05$), whereas difference between group 2 and group 3 was not significant ($p > 0.05$)
(‡): Differences between group1 and group2, group 1 and group 3, and group 2 and group 3 were significant ($p < 0.05$)

4. Discussion

Lead, both in organic and inorganic forms, is a serious environmental and health problem. In adults, about 10% of ingested lead is absorbed from the gastrointestinal tract [5]. Once absorbed, lead accumulates in three compartments: blood, soft tissues and especially in bones, where it can be stored for years [11]. Factors that affect calcium distribution also affect lead distribution [6]. The lead circulating in the bloodstream is mobile, in contrast to that stored in bones and it is this lead that exerts adverse effects on the body [7]. For this reason, the concentration of lead in the blood is an important parameter in the characterization of a person's exposure to lead [7]. Lead can cause hematological, gastrointestinal, rheumatological, endocrine, neurological and renal problems in humans [6-8,11].

Lead can cause damage to cell membranes and can adversely affect oxido-reductive processes in cells. Effects can be seen at the sub cellular level range from inhibition of enzymes to the production of marked morphological changes [7].

Effects of lead on thyroid functions have been under investigation for more than 50 years. Slingerland's study in 1955 first provided evidence that the thyroid glands had diminished iodine uptake in lead-exposed individuals [12]. Sandstead's study in 1969 [14] confirmed the results of that early study. Tuppurainen et al. [15] suggested that lead has effects on both peripheral thyroid hormone levels and on thyroid stimulating hormone (TSH) levels. More recently, Singh et al. [7] showed adverse effects of lead on the pituitary-thyroid axis.

In lead-exposed workers, we observed a significant rise in serum sTSH levels despite normal fT3 and fT4 levels. This is consistent with the findings of Gustafson et al. [16] who observed a dose-related depression of thyroid functions during occupational exposure to inorganic lead despite normal fT3 and fT4 levels. Also, sTSH levels in our lead-exposed workers were higher than in the control group. The sTSH rise was independent of lead exposure time but was related to blood lead levels. These results suggest that higher levels of lead can cause more marked changes in thyroid physiology. On the other hand, sTSH levels were high in all three groups having different blood lead levels, and this indicates that lead exposure may alter thyroid physiology even at low doses. Differences of fT3 and fT4 levels according to the blood lead levels were also significant. sTSH and fT3, fT4 levels were observed high with high blood lead levels. This results indicates that lead in high levels alters thyroid functions more excessively. Therefore, in cases of lead exposed situations, having high blood lead levels should be evaluated more attentively.

Tuppurainen et al. [15] and Refowitz [17] reported no relationship between blood lead levels and T4 or fT4, as well as no thyroid abnormalities in subjects who were exposed to lead. Our fT3 and fT4 results are in agreement with these studies.

Liang et al. [18] reported that high levels of lead in the blood caused inhibition of deiodinization of T4 and disruption of thyroid physiology, but found no correlation with lead exposure times [18]. Similarly, we did not find any correlation between sTSH levels and lead exposure time.

In the current literature, there is no consensus regarding the effects of lead on thyroid physiology. A possible source for the diversity of findings might be differences in the intensity of exposure to lead in different individuals, apart from differences in exposure time.

In our lead-exposed patients, sTSH levels were significantly higher than in the control group, but we observed no other systematic differences. This suggests that lead might cause subclinical alterations in thyroid physiology which cannot be measured by fT3 and fT4 levels but which manifest as alterations in TSH levels. This possibility could be analyzed further with detailed morphological, biochemical and molecular studies.

As a result, not only specialists who are interested in the thyroid gland but other clinicians as well should be aware of the potential hazardous effects of lead on the gland, especially in patients who have been occupationally exposed to lead.

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