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Study the Effects of Lead on Thyroid Functions in Alexandria Occupationally Exposed Workers

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Abstract
This study aimed to explore the effects of lead on the thyroid function of Alexandria occupationally exposed workers. One hundred male workers occupationally exposed to lead in a factory for bullets and shots were investigated. The level of blood lead was measured by atomic absorption spectro photometry .Thyroid-stimulating hormone, free thyroxine, free triiodothyronune and anti thyroid peroxidase in serum were estimated by enzyme immunoassay. Thyroid ultrasound was performed by an expert radiologist using 5-10HZ probe device.
The workers with higher level of blood lead (40-60 micrograms/dl) showed high Thyroid-stimulating hormone level (0.81 – 9.30 mIU/ml) and abnormal ultrasound findings; volume and echo texture changes. No changes in free thyroxine, free triiodothyronune and anti thyroid peroxidase were observed. We concluded that higher level of blood lead may cause certain damage to thyroid function leading to subclinical hypothyroidism, with no evidence of thyroid immune dysfunction.
Key words: *Thyroid diseases, Lead, Occupational exposure.*

Introduction

The incidence of thyroid disorders is increasing all over the world. This high incidence suggested that there are hidden factors of thyroid disorders.[1] there may be a connection between occupational exposure to certain toxic substances and thyroid diseases, including cancer and autoimmune thyroid disorder.[2] Among these toxic substances that affect thyroid functions are perchlorate[3], thiocyanate[3], DDT[4] and lead. [5] Lead is a

chemical element in the carbon group. Due to its corrosion-resistive property, the uses of lead have grown to a wider aspect. Lead, in one form or the other, is present all round us. [6] Occupational exposure is the main cause of lead poisoning.[7] People can be exposed when working in facilities that produce a variety of lead-containing products; these include radiation shields, ammunition, certain surgical equipment, fetal monitors, plumbing, circuit boards, jet engines, and ceramic glazes.[8] Once in the body, small amount of lead travels in the blood to soft tissues such as the liver, kidneys, lungs, brain, spleen, muscles, and heart. Lead is a health risk factor leading after high-grade exposure to poisoning. It is rapidly absorbed into the bloodstream then accumulates in the body and exerts toxic effects especially on the central nervous system, the cardiovascular system, kidneys and the endocrine system. [9]

The primary cause of lead's toxicity is its interference with a variety of enzymes because it binds to sulfhydryl groups found on many enzymes.[10] Part of lead's toxicity results from its ability to mimic other metals that take part in biological processes, which act as cofactors in many enzymatic reactions, displacing them at the enzymes on which they act.[9] Among the essential metals with which lead interacts are calcium, iron, and zinc.[11]

Thyroid hormone kinetics are affected by lead. Central defect of the thyroid axis or an alteration in T4 metabolism or binding to proteins may be involved in derangements in thyroid hormone action. [12]Moreover, it has been suggested that the nonspecific symptoms of inorganic lead intoxication are related to the effects of the blood lead on thyroid function. [13]

Materials and methods

The present study included one hundred subjects occupationally exposed to lead in a factory for bullets and shots in Alexandria. Because few female workers were assigned to lead-exposed production areas, only male workers were recruited. Age of the study subjects was in the range of 16-49 years old and exclusion criteria were past history or family history of thyroid disorders, diabetes mellitus, drugs that affect thyroid function and smoking. The study subjects were classified according to the blood level of lead into 3 groups:

Group I: 10-25 Micrograms/dl

Group II: 26 -40 micrograms/dl

Group III: 41-60 micrograms/dl

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 heparinized lead-free tubes. Collection of samples was done in a lab near the target factory and transported in an ice box to the central lab.

Lead was measurd by AA 6650 Shimad ZU atomic absorption spectrophotometer using Nitric acid and Perchloric decomposition and precipitation of proteins. The results were obtained as µg/dl. [14]

Serum thyroid hormone profile:

Venous blood samples were collected aseptically without additives, stored at 18-25C for 15-45minutes then centrifuged to obtain the serum specimens which were stored at 2-8C to be analyzed at the second day. Measurement of serum free triiodothyronine (fT3) and free thyroxine (fT4) by (competitive enzyme immunoassay), serum TSH by (a tow- site immunoenzymometric assay) and serum ATPO using a solid- phase, enzyme –labeled, chemiluminescent sequential immunometric assay). All measurements were done with TOSOH AIA 21 analyser(TOSOH Corporation, Tokyo, Japan) using the TOSOH reagents. [15,16]

Thyroid ultra sound:

High resolution ultra sonography of the thyroid gland was done by an expert radiologist using 5-10HZ probe device ,TOSHIBA xaria high end device using xaria for both gray scale and duplex assessment of the thyroid gland.

Results

Demographic data:

The three 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 $p < 0.05$. The mean age for group I was 34.11 years, the mean age for group II was 33 years and the mean age for group III was 31.54 years. There was no significant difference between the 3 groups regarding age.

The mean duration of exposure of group I was7.74 years, the mean duration of exposure of group II was 7.44 years and the mean duration of exposure of group III was7.92 years. There was no significant difference between the three groups regarding duration of exposure. The mean BMI of group I was 26.83 kg/m^2, and that of group II was 26.10 kg/m^2 while that of group III was26.42 kg/m^2. There was no significant difference between the three groups regarding BMI.

Thyroid function tests:

The mean value of FT3 in group I was 2.91 Pg/ml, in group II was3.08 Pg/ml and in group III was 3.14 Pg/ml. there was no significant difference between the 3 groups according to FT3.The mean value of FT4 in group I was 1.19 ng/dl, in group II was 1.25 ng/dl and in group III was 1.33 ng/dl. There was no significant difference between the 3 groups according to FT4.The mean value of TSH in group I was 1.84 uIU /ml, in group II was1.81 uIU /ml and in group III was 5.83 uIU/ml. The mean serum TSH was significantly higher in group III in comparison to group I and II. The mean value of ATPO in group I was 17.29IU/ml and in group II was 15.43 IU/ml while in group III was17.31 IU/ml. There was no significant difference between the 3 groups according to ATPO.

Thyroid ultra sound

Comparison of U/S finding of three the studied groups revealed many abnormalities regarding size and texture. Enlarged volume was found in 5.3% of group I, 27.8% of group II and 30.8% of

group III with Significant difference between group I and II and between group I and III.Enlarged isthmus was found in 15.8% of group I, 38.9% of group II and 46.2% of group III with Significant difference between group I and II and between group I and III.Cysts and nodules were found in26.3% of group I, 39% of group II and 61.6% of group III with Significant difference between group I and II, between group I and III and between group II and III.Coarse echo texture was found in10.5% of group I, 38.9% of group II and 46.5% of group III with Significant difference between group I and II and between group I and III.No calcification or Doppler changes were found in all the study subjects.

Discussion

The results of our study revealed that there is significant difference between group I and III and between group II and III regarding TSH. No significant difference between the three groups regarding FT3, FT4or ATPO. Regarding thyroid U/S, all the 3 groups showed many abnormalities regarding size and texture with the presence of multiple or solitary thyroid nodules. Group III had the highest percent of U/S abnormalities and there was significant statistical difference between group I&II, II&III and I&III. These laboratory and radiological changes suggest that lead causes primary sub-clinical hypothyroidism due to direct damage to the thyroid gland.

Several studies have evaluated the effects of lead on thyroid hormone levels in occupationally exposed workers.

Baljinder Singh, et al 2000, found that no significant alteration was observed in the mean T3 and T4 levels of exposed workers. On the other hand, there was a rise in TSH associated with increasing levels of blood lead.

The similarities between our study and this study may be attributed to the near ranges of BLL of both study subjects. The difference between the two studies in T3may be because our study measured Ft3 while Baljinder Singh measured total T3. This is likely explainable by variations in thyroid-binding capacity. [17]

Recep Pekcici1, etal.2009 who retrospectively examined the records of 65 men who had been exposed to lead while working as automotive mechanics or in battery factories, classified the lead-exposed workers into three groups according to their blood lead levels, as follows: 40 - 59 µg/dl, 60 - 79 µg/dl, or 80 µg/ dl and above. TSH levels were high in all three groups having different blood lead levels, Differences of fT3 and fT4 levels according to the blood lead levels were also significant. TSH and fT3, fT4 levels were observed high with high blood lead levels>80 µg/dl. This result indicates that lead in high levels alters thyroid functions more excessively. [18]

C. M. L ´ OPEZ 2000 investigated a total of 75 males working in a factory making lead batteries that were exposed to lead for over 2 and up to 8 years. There was no statistically significant correlation between PbB and thyroid hormones and TSH in the whole population examined (PbB range 8–98 µg/ dl). [19]

These discrepancies between our present study and C. M. L ´ OPEZ could be due to the fact that

he studied exclusively and globally the total PbB–hormone ranges of the populations without keeping in mind the different PbB levels which diversely affect hormonal levels, while in our study we classified and investigated every group according to PbB levels.

L IANG Qi-rong et al. 2003 investigated 157 workers occupationally exposed to lead in a smelting factory to explore the effects of lead on the thyroid function of occupationally exposed workers. The concentration of lead in air at workshop was measured by flame atomic absorption spectrophotometry(FAAS) and the levels of blood lead(PbB) by atomic absorption spectrophotometry (AAS) ,as well as TSH, T3, T4 ,FT3 and FT4 in serum by radioimmunoassay. The workers with higher level of blood lead showed lower levels of T3and FT3than those with lower blood lead level. This study supports the idea that higher level of blood lead may cause certain damage to thyroid function by inhibiting de-iodination of T4. [20]

Conclusions

Lead causes abnormal changes in thyroid gland structure in workers who are occupationally exposed to lead. These changes lead to impaired thyroid function as seen by increase serum TSH level in spite of normal FT3 and FT4. All these effects of lead are not related to the duration of exposure.

Table (I): Comparison between the studied groups according to demographic data and BMI.

	Group I (n = 38)		Group II (n = 36)		Group III (n = 26)		Total (n=100)	
	No.	%	No.	%	No.	%	No.	%
Age/year								
Min. – Max.	19.0 – 49.0		16.0 – 45.0		18.0 – 49.0		16.0 – 49.0	
Mean ± SD	34.11 ± 9.22		33.0 ± 7.77		31.54 ± 9.67		33.04 ± 8.82	
Median	35.0		35.0		30.0		35.0	
$^{KW}\chi^2$ (p)	1.411 (0.494)							
Duration of exposure/year								
Min – Max	1.0 – 20.0		1.0 – 20.0		2.0 – 21.0		1.0 – 21.0	
Mean ± SD	7.74 ± 4.93		7.44 ± 4.37		7.92 ± 5.80		7.68 ± 4.94	
Median	7.0		7.0		6.0		7.0	
$^{KW}\chi^2$ (p)	0.050 (0.975)							
BMI(kg/ m^2)								
Min. – Max.	18.87 – 31.70		19.20 – 38.10		18.87 – 30.90		18.87 – 38.10	
Mean ± SD	26.83 ± 3.74		26.10 ± 4.62		26.42 ± 3.10		26.46 ± 3.91	
Median	27.87		26.88		26.14		27.66	
F (p)	0.315 (0.730)							

Group I:BLL: 10-25 micrograms/dl, Group II: 26 -40 micrograms/dl and Group III: 41-60 micrograms/dl.

Table (II): Comparison between the studied groups according to thyroid function tests.

	Group I (n = 38)	Group II (n = 36)	Group III (n = 26)	Total (n=100)
FT3 Pg/ml				
Min – Max	2.25 – 3.40	2.25 – 3.80	2.25 – 3.90	2.25 – 3.90
Mean ± SD	2.91 ± 0.36	3.08 ± 0.39	3.14 ± 0.49	3.03 ± 0.42
Median	3.0	3.10	3.10	3.10
F (p)	3.042 (0.052)			
FT4 ng/dl				
Min – Max	0.82 – 1.82	0.87 – 2.0	0.92 – 1.82	0.82 – 2.0
Mean ± SD	1.19 ± 0.30	1.25 ± 0.36	1.33 ± 0.30	1.25 ± 0.33
Median	1.11	1.13	1.30	1.13
$^{KW}\chi^2$ (p)	4.151 (0.125)			
TSH mIU/ml				
Min – Max	0.03 – 3.0	0.91 – 5.0	0.81 – 9.30	0.03 – 9.30
Mean ± SD	1.84 ± 0.82	1.81 ± 1.04	5.83 ± 2.72	2.87 ± 2.37
Median	2.0	1.36	6.50	2.11
$^{KW}\chi^2$ (p)	28.579* (<0.001)			
Sig. bet. groups$^{@}$	I-III***,II-III***			
ATPO IU/ml				
Min – Max	2.60 – 49.30	1.20 – 33.0	6.0 – 34.0	1.20 – 49.30
Mean ± SD	17.29 ± 11.26	15.43 ± 10.21	17.31 ± 9.84	16.63 ± 10.46
Median	11.30	10.75	13.0	12.50
$^{KW}\chi^2$ (p)	2.502 (0.286)			

Group I:BLL: 10-25 micrograms/dl, Group II: 26 -40 micrograms/dl and Group III: 41-60 micrograms/dl.

Table (III):Comparison between the studied groups according to thyroid gland ultrasound finding.

	Group I (n = 38)		Group II (n = 36)		Group III (n = 26)		Total (n=100)	
	No	%	No	%	No	%	No	%
Enlarged lobes volume	2	5.3	10	27.8	8	30.8	20	20.0
χ^2 (p)	8.404* (0.015)							
Sig. bet. groups	I-II**, I-III*							
Enlarged isthmus volume	6	15.8	14	38.9	12	46.2	32	32.0
χ^2 (p)	7.768* (0.021)							
Sig. bet. groups	I-II*,I-III**							
Cysts nodules	10	26. 3	12	39	16	61.6	40	40
χ^2 (^{MC}p)	23.514* (0.001)							
Sig. bet. groups	I-II*,I-III**,II-III**							
Coarse cho texture	4	10.5	14	38.9	12	46.2	30	30.0
χ^2 (p)	11.447* (0.003)							
Sig. bet. grps	I-II**,I-III**							

Group I:BLL: 10-25 micrograms/dl, Group II: 26 -40 micrograms/dl and Group III: 41-60 micrograms/dl.

$^{KW}\chi^2$: Chi square for Kruskal Wallis test F: F test (ANOVA)

#:Sig. bet. grps was done using Post Hoc Test (Scheffe) ***: Statistically significant at p ≤ 0.001

*: Statistically significant at p ≤0.05 **: Statistically significant at p ≤ 0.01

@:Sig. bet. grps was done using Mann Whitney test

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