ORIGINAL ARTICLE

Evaluation of the effects of chronic exposure to organophosphorus pesticides on thyroid function

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Abstract

Background: Organophosphorus (OP) compounds are considered among the most common insecticides. The major mechanism of organophosphorus toxicants includes inhibiting cholinesterase enzyme. organophosphorus toxicants cause impaired thyroid hormones through affecting different parts of the hypothalamus-pituitary-thyroid axis. The aim of this study is to determine the effects of chronic exposure to organophosphorus pesticides on thyroid function.
Methods: The present descriptive-analytical study was conducted cross-sectionally on male workers employed in a factory producing OP as the exposure group as well as the personnel of the administrative department of the same factory as the control group chosen through census method. According to Helsinki declaration, 5 ml of venous blood was collected, and the activity of TT_3, TT_4, FT_3, FT_4, and TSH hormones was measured through CLIA method, while the activity of serum cholinesterase enzyme (CHE) was measured through colorimetry.
Results: T-test indicated that there was no significant difference in the mean of activity of hormones and enzyme studied between exposure and control groups ($p>0.05$). Nevertheless, the activity of TT_3, TT_4, FT_3, FT_4 hormones, and CHE enzyme was lower in the exposure group, while that of TSH was higher than in the control group. Pearson correlation test indicated that there was no significant correlation between the activity of all studied hormones and CHE enzyme ($p>0.05$).
Conclusions: In the present study, the workers employed in the factory producing OP did not suffer thyroid disorders. Further, OP did not have a considerable effect on the activity of CHE enzyme.

Keywords: Organophosphorus Compounds, Cholinesterase, Hormones, Thyroid Gland, Endocrine Glands

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INTRODUCTION

So far, humans have employed different methods for controlling pests, one of which is use of pesticides. The most important damages caused by pests are observed on agricultural crops as well as food, industries, and human health. Therefore, concerning the harmful effects of pests and absence of more suitable methods, use of pesticides seems to be essential as the most effective, rapid, and inexpensive method [1, 2]. According to the definition by Federal Insecticide Fungicide and Rodenticide Act (FIFRA), a pesticide refers to any substance or compound used for preventing, killing, repelling, or mitigating pests [1]. The term pest refers to any harmful plant, animal, and microorganism [1]. According to studies, developing countries claim 85% of global production of pesticides, such that around 20-25 thousand tons per year and around 0.5% of the global consumption are related to Iran [3].

Among pests, insects are considered the most important because of the diversity of species, multiplicity of the species population, and other factors. Since insects have biochemical similarities (nervous system and neurotransmitter enzymes) with a human, and as the function of pesticides is nonselective and does not affect only special creatures or targets, therefore these pesticides can engender detrimental effects in humans [4]. One of the most important and common pesticides are organophosphorus compounds [5]. In Iran, organophosphorus poisoning has been reported as the third cause of poisoning and the main cause of mortality caused by poisoning [6]. Organophosphorus pesticides are compounds which have phosphorus in their structure [5].

In these compounds, there is a double bond between phosphorus with (sulfur or oxygen) and a single bond between phosphorus with the X group. X group refers to the leaving group. Pentavalent phosphorus enables establishing a double bond with one oxygen or sulfur (S=O is able to inhibit esterases) [7]. Most organophosphorus insecticides have a similar toxicokinetics and similar mechanism of action. They

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have also a nonpolar and lipid soluble structure [4, 7].

The mechanism of action of these compounds is inhibiting cholinesterase enzymes. According to 80 years of research, in the presence of Acetyl cholinesterase (AChE) and Butyryl Choline esterase (BChE), Acetyl choline (ACh) is hydrolyzed. In other words, ACh (neurotransmitter) is degraded into acetic acid and choline, thereby stopping neurotransmission in synapses. When these enzymes are inhibited, neurotransmission operations are not dampened, whereby an extreme and stable excitation occurs in the nervous system [4, 8, 9]. ACh is released when the neurotransmitter is transmitted from one neuron to muscles, endocrine cells, and others [10]. One of the best ways for determining the extent of contact and effects of chemicals in humans is biological monitoring [6]. Biological monitoring refers to the monitoring of existence of any toxic chemical or its metabolites in tissues or body fluids (exposure biological monitoring) or monitoring of the effects of chemicals and incidence of pathological and biological changes (biological monitoring of effects). Biological monitoring captures the internal dose of a substance in the body. Further it also assesses the uptake and entrance of toxins to the body through all possible routes (skin, inhalation, digestion, etc.). Therefore, it can offer a more proper assessment of health threatening risks compared to measuring the environmental concentration of pollutants [11]. For organophosphorus pesticides, the simplest and most effective method for biological monitoring of effects is cholinesterase enzyme which is inhibited and blocked by these toxins [5].

Thyroid hormones play a significant role in preserving homeostasis, regulating energy consumption, stimulation, metabolism, and activity of cells. The most important effects of thyroid hormones include genetic effects, oxygen uptake stimulation, growth and development in mammals, regulating lipid metabolism, increasing uptake of carbohydrates from the intestines, increasing the production of 2,3-bisphosphoglycerate, and releasing oxygen from hemoglobin. Further, these hormones also affect the cardiovascular, nervous, musculoskeletal, and other systems [12, 13].

Recently, pesticides have been identified and classified as endocrine disrupting chemicals (EDCs) [14]. Nevertheless, investigation and studies have suggested contradictory effects of these chemicals on the thyroid gland especially among men. Therefore, currently the relationship between use of pesticides and hypothyroidism is unknown and ambiguous [15].

Organophosphorus toxicants cause impaired thyroid hormones through affecting different parts of the hypothalamus- pituitary- thyroid axis, i.e. the hormone receptors, synthesis of hormones, as well as their secretion and metabolism [14]. The possible mechanisms of the effect of organophosphorus toxicants on thyroid hormones are categorized into direct and indirect effects. Interfering in the binding of transport proteins to thyroid hormones [16], interfering in binding of thyroid hormones to their receptors (TH-r) in target cells [14], interfering in the binding of TSH hormone to its receptors (TSH-r) in thyroid and inhibiting the synthesis of thyroid hormones [14], disrupting the function and activity of deiodinase and thyroid peroxidase enzymes [17], inhibiting iodine uptake through sodium-iodide symporter [15], interfering in the mechanism of cellular uptake of thyroid hormones [16], changing and interfering in thyroid gene expression which is the mediator for thyroid hormone production [18], and increasing clearance of thyroid hormones [17] are among the most important mechanisms of the direct effect of organophosphorus pesticides on thyroid hormones. The controlling mechanisms of release of hormones include four major groups of neural, hormonal, nutritional, and environmental factors, which regulate the plasma level of hormones. The central nervous system (CNS) is one of the most important components of regulation of release of hormones as well as controlling and integrating them, through which the release of hormones is directly controlled by neurotransmitters.

On the other hand, the release of hormones from endocrine cells can be regulated and modified by postganglionic neurons of the parasympathetic nervous system (PSNS) and sympathetic nervous system (SNS) which use acetylcholine (ACh) or norepinephrine (NE) as neurotransmitters or directly by preganglionic neurons which use Ach as neurotransmitter. Therefore, drugs and chemicals which interact with the production and release of neurotransmitters (such as organophosphorus toxicants causing inhibition of cholinesterase and resulting in accumulation of ACh) indirectly affect the endocrine function [13]. Note that one of the other mechanisms of the indirect effect of organophosphorus toxicants on thyroid hormones occurs through disrupting the function and activity of liver through failure in production and metabolism of transport proteins in the liver as well as impairing the detoxification, biotransformation, and metabolism processes [11, 13].

Contact with pesticides occurs through occupational and environmental exposure. The workers employed in factories that produce pesticides, farmers, gardeners, pesticide applicators, and researchers are among the most important occupational groups exposed to these toxicants. The workers employed in factories that produce and prepare pesticides harbor a greater risk for developing complications and adverse effects of exposure to pesticides because of their longer exposure and higher concentration compared to other occupational environments and professions [4, 5]. Furthermore, most present studies have been performed on other occupational groups exposed to pesticides. The present study was performed to determine the effects of chronic exposure to organophosphorus pesticides on thyroid function.

METHODS

This analytical-descriptive study was performed cross-sectionally on workers employed in a factory as exposure group as well as the personnel of the administrative department of that factory as the control group. The studied population consisted of male workers employed in a factory producing organophosphorus pesticides. The sample size in the exposure and control groups was chosen based on census method. Further, the control group (nonexposed) was matched with an exposure group in terms of working background, height, weight, body mass index (BMI), level of income, and type of employment. The inclusion criteria were

complete consent to participate in the study, not having any thyroid disease (hypo- or hyperthyroidism), not using thyroid-interfering drugs (Glucocorticoids, Lithium, Amiodarone, Interferon-α, Rifampin, ...), use of personal protection equipment (PPE), having six months of working background with organophosphorus toxicants (exposure group), and not having history of exposure to these substances (control group). The required information was obtained through investigating the medical records (annual and periodic tests) and drug history, occupational medicine examinations, demographics questionnaire, and interview with the person.

For taking the blood samples, first after presenting the necessary explanations and training to the participants, based on Helsinki declaration (Version 2013) [19], 5 ml of venous blood was taken by a skillful and experienced person from the participants in this study. Then, the serum of samples was separated by a 16-branch centrifuge device (Lab Trone co., Iran) at 3100 rpm within 13 min. After aliquoting, they were stored at -20 °C. In order to measure the activity of TT_3 (total tri iodothyronine), TT_4 (total tetra iodothyronine), TSH (thyroid stimulating hormone), and FT_4 (free tetra iodothyronine) hormones, kits with the catalog numbers of L2KT36, K2KT46, L2KTS6, and L2KTF42 were used respectively through Chemi Luminescence Immuno Assays (CLIA) via IMMULITE 2000 device (Siemens Co., USA). On the other hand, for FT_3 hormone (free tri iodothyronine), the mentioned method was used with the catalog number of 131-5589, VITROS ECIQ device (ORTHO Co., USA) based on the manufacturer's protocol. Furthermore, in order to measure the activity of serum cholinesterase enzyme (CHE) [Ec 3.1.1.8], a kit with the catalog number of AD039 (Audit Diagnostics Co., Ireland) was used via colorimetry through AutoAnalyzer device (Hitachi 917, Japan). Eventually, the studied data were analyzed via SPSS 21 through descriptive statistics, T-test, one-way ANOVA and Pearson correlation.

RESULTS

This study was performed on 41 subjects (26 in the exposure group and 15 in the control group) of the workers employed in a factory producing organophosphorus pesticides within the age range of 22-52 years and working background of 1-25 years. Based on the obtained results, there was no significant difference between the demographic characteristics of the workers of the factory in terms of working background, height, weight, BMI in the exposure and control groups ($p>0.05$). Furthermore, all of the workers of the exposure group used personal protection equipment (PPE) in their workplace. The supplementary information regarding the demographics of factory workers is presented in Table 1.

T-test indicated that there was no significant difference in the mean activity of TT_3, TT_4, TSH, FT_3, FT_4 hormones and CHE enzyme between exposure and control groups ($p>0.05$). Nevertheless, the activity of TT_3, TT_4, FT_3, FT_4 hormones, and CHE enzyme was lower in the exposure group, while that of TSH was higher than in the control group. Pearson correlation test showed that there was no significant correlation between the activity of all hormones of study and CHE enzyme ($p>0.05$). Extra details regarding the results of T-test and Pearson correlation test are presented in Tables 2 and 3, respectively.

One-way ANOVA test revealed that in the exposure group, there was a significant difference between the mean activity of FT_3 and age group ($p<0.05$); this difference was observed between the age groups of 20-30 and 30-40. Further, based on T-test results, no significant difference was observed across different age groups regarding the mean activity of all studied hormones and CHE enzyme between the exposure and control groups ($p>0.05$). Extra details regarding the results of these tests are reported in Table 4.

One-way ANOVA test also showed that there was no significant difference between the mean activity of all hormones as well as CHE and the working background ($p>0.05$). On the other hand, based on the results of T-test, in those with 10-20 years of work experience, the mean activity of CHE significantly decreased in the exposure group compared to the control ($p<0.05$). Extra information about the results of analysis of variance and t-test is provided in Table 4.

According to the T-test results, in smokers the mean activity of FT_3 for the exposure and control groups was obtained as 6±0.38 and 7.32±0.98 respectively, where this difference was statistically significant ($p<0.05$). Extra

Table 1. Demographics of the participants of the study

Variable	Mean ± SD		P-value
	Exposure group	Control group	
Age (years)	37.33 ± 7.36	42.33 ± 8.3	0.048*
Working background (years)	13.05 ± 7.87	16.66 ± 7.63	0.161
Height (cm)	175.23 ± 8.05	175.46 ± 7	0.925
Weight (kg)	77.5 ± 13.52	79.13 ± 13.2	0.709
Body Mass Index (BMI)	25.22 ± 4.08	25.61 ± 3.73	0.765
Smoking		Percentage	
Yes	38.5 %	6.7 %	0.027*
No	61.5 %	93.3 %	(Chi-Square)

* P-Value<0.05, ** P-Value<0.01

Table 2. The mean and standard deviation of the studied parameters

Variable	Mean ± SD		P-value	Reference Values
	Exposure group	Control group		
TT_3 (ngr/ml)	1 ± 0.2	1.08 ± 0.23	0.241	0.84 - 1.72
TT_4 (µgr/dl)	7.89 ± 1.87	8.34 ± 1.69	0.452	4.5 - 12.5
TSH (µIu/ml)	2.7 ± 1.32	2.32 ± 1.64	0.45	0.4 - 4
FT_3 (Pmol/l)	5.86 ± 0.52	6.1 ± 0.98	0.395	4.26 - 8.1
FT_4 (Pmol/l)	15.16 ± 2.82	15.44 ± 2.77	0.756	11.5 – 22.7
CHE (U/L)	8531.46 ± 1885.735	9034.6 ± 951.07	0.264	5100 - 11700

TT3: total tri iodothyronine, TT4: total tetra iodothyronine, TSH: thyroid stimulating hormone, FT3: free tri iodothyronine, FT4: free tetra iodothyronine, CHE: cholinesterase enzyme, * P-Value<0.05, ** P-Value<0.01

Table 3. The results of Pearson correlation test between the studied hormones and cholinesterase enzyme

		Hormone					
			TT_3	TT_4	TSH	FT_3	FT_4
CHE Enzyme	Exposure group	r	0.056	- 0.042	0.202	- 0.057	- 0.182
		P-Value	0.785	0.839	0.333	0.783	0.374
	Control group	r	- 0.098	- 0.107	- 0.211	- 0.172	- 0.188
		P-Value	0.729	0.705	0.450	0.540	0.501

TT3: total tri iodothyronine, TT4: total tetra iodothyronine, TSH: thyroid stimulating hormone, FT3: free tri iodothyronine, FT4: free tetra iodothyronine, CHE: cholinesterase enzyme, r: Correlation, * P-Value<0.05, ** P-Value<0.01

information about the results of this test is summarized in Table 5.

Based on T-test results, smoking had no significant effect on the activity of cholinesterase in the exposure or control groups. Further, in terms of occupational group (exposure and control), exposure to organophosphorus toxicants did not have any significant effect on the mean activity of cholinesterase between smokers and non-smokers ($p>0.05$). Extra details regarding the results of this test are demonstrated in Figure 1.

DISCUSSION

In the present study, the mean activity of TT_3, TT_4, FT_3, FT_4 hormones as well as CHE enzyme was lower in the exposure group, while that of TSH was higher compared to the control, though these differences were not statistically significant. Therefore, it can be stated that in the present study, the male workers employed in the factory producing organophosphorus pesticides have not developed hypothyroidism. Furthermore, organophosphorus toxicants have not had a considerable effect on the activity of CHE. Based on the investigations and visits of the factory, the halls of the production line are equipped with ventilation system, and all of the workers employed in the factory utilize personal protection equipment including mask and gloves in the workplace. In the studied factory, the workers do not operate constantly and permanently in a single occupational unit; rather, they work rotationally across different units of the factory including packaging, formulation, and others. Further, in the halls of the production line, the ceiling is very high, and the space and width of the workplace are very large, thereby preventing accumulation of contamination in the workplace. Accordingly, based on the mentioned reasons, it seems that the workers have less exposure to organophosphorus toxicants and the dose uptake in the body can be minimized.

In addition to the mentioned reasons, another important reason of the above results is associated with the nature of the toxins produced by the factory. This factory produces four organophosphorus pesticides including Diazinon, Chlorpyrifos, Malathion, and Ethion; these toxicants belong to Phosphorothioate and Phosphorodithioate groups. In the chemical structure of the mentioned insecticides, there is a double bond between phosphorus and sulfur, and these compounds have less power in inhibiting cholinesterase compared to toxins with double phosphorus-oxygen bond [11].

In the study by Zaidi et al. similar to this study, the activity of T4 and TSH differed in workers dealing with formulation of pesticides and control group; the mean activity of T4 and TSH in the exposure group was 8.92±2.36 and 3.68±2.43, while in the control group the values were 9.58±1.42 and 2.88±0.51, respectively, though this difference was not statistically significant [20].

In the study by Manfo et al. on male farmers of one of the Western cities of Cameron, similar to this study, no significant

Table 4. The results of the one-way ANOVA test and independent sample T-test

		TT_3 (ngr/ml)			TT_4 (µgr/dl)			TSH (µlu/ml)			FT_3 (Pmol/l)			FT_4 (Pmol/l)			CHE (U/L)		
		exposure	Control	P-value[a]	exposure	Control	P-value[a]	exposure	Control	P-value[a]	exposure	Control	P-value[a]	exposure	Control	P-value[a]	exposure	Control	P-value[a]
Age groups (years)	20-30	0.91 ± 0.11	1.08 ± 0.14	0.09	7.77 ± 1.94	8.66 ± 0.9	0.48	3.36 ± 0.76	2.14 ± 1.96	0.347	6.28 ± 0.43	6.1 ± 1.05	0.803	16.21 ± 4.24	15.73 ± 1.85	0.86	7595.33 ± 2418.865	9015 ± 1054.9	0.523
	30-40	1 ± 0.2	1 ± 0.08	0.954	7.9 ± 1.3	8 ± 0.85	0.996	1.61 ± 0.5	3.61 ± 2.16	0.432	5.46 ± 0.5	6.66 ± 1.02	0.063	13.45 ± 1.09	15.8 ± 1.5	0.093	9364.714 ± 1946.92	8229 ± 980.05	0.605
	40-50	1.04 ± 0.23	1.09 ± 0.3	0.625	7.96 ± 2.21	8.22 ± 2.08	0.78	2.43 ± 1.52	1.8 ± 0.82	0.226	5.9 ± 0.43	6.09 ± 1.16	0.63	15.6 ± 2.46	15.47 ± 3.51	0.93	8346.84 ± 1571.496	9026.77 ± 952.9	0.262
	>50	-	1.08 ± 0.08	-	-	8.61 ± 1.68	-	-	3.47 ± 0.63	-	-	5.87 ± 0.04	-	-	14.7 ± 0.7	-	-	9502 ± 1443.9	-
	P-value[b]	0.463	0.986	-	0.98	0.973	-	0.073	0.523	-	0.011*	0.943	-	0.16	0.984	-	0.375	0.776	-
Working background (years) (years)	1-10	0.93 ± 0.15	1.06 ± 0.13	0.142	7.9 ± 1.62	8.47 ± 0.82	0.526	2.92 ± 1.07	2.65 ± 2.24	0.822	5.9 ± 0.64	6.24 ± 0.9	0.423	15.08 ± 3.36	15.75 ± 1.51	0.713	8691.18 ± 2341.16	8818.5 ± 946.74	0.919
	10-20	1.05 ± 0.24	1.16 ± 0.22	0.358	7.6 ± 2.36	9.04 ± 2.25	0.235	1.93 ± 1.37	1.9 ± 0.98	0.948	5.72 ± 0.42	6.3 ± 1.26	0.195	15.1 ± 2.8	16.25 ± 4.07	0.5	8072.63 ± 1413.03	9539 ± 864.15	0.036*
	20-30	1 ± 0.2	1.01 ± 0.33	0.76	8.74 ± 0.71	7.4 ± 1.12	0.078	3.44 ± 1.13	2.46 ± 0.9	0.202	6.17 ± 0.24	5.78 ± 0.75	0.359	15.55	14.24 ± 1.2	0.202	9354 ± 1712.7	8061.6 ± 946	0.427
	P-value[b]	0.305	0.61	-	0.586	0.292	-	0.578	0.158	-	0.334	0.702	-	0.96	0.506	-	0.493	0.244	-

TT_3: total tri iodothyronine, TT_4: total tetra iodothyronine, TSH: thyroid stimulating hormone, FT_3: free tri iodothyronine, FT_4: free tetra iodothyronine, CHE: cholinesterase enzyme, a: independent sample T-test, b: one-way ANOVA, * P-Value<0.05, ** P-Value<0.01

Table 5. The mean and standard deviation of the activity of the studied hormones in terms of smoking

Variable	Group	Smoking		P-value
		Yes	No	(T-test)
	exposure	1 ± 0.24	1.01 ± 0.18	0.811
TT_3 (ngr/ml)	Control	1.21 ± 0.2	1.07 ± 0.24	0.613
	T-test (P-value)	0.4	0.409	-
	exposure	7.66 ± 2.03	8.04 ± 1.82	0.616
TT_4 (µgr/dl)	Control	7.65 ± 1.6	8.4 ± 1.74	0.687
	T-test (P-value)	0.997	0.601	-
	exposure	3.2 ± 1.1	2.66 ± 1.36	0.25
TSH (µIu/ml)	Control	1.85 ± 073	2.63 ± 1.2	0.718
	T-test (P-value)	0.116	0.958	-
	exposure	6 ± 0.357	5.77 ± 0.6	0.281
FT_3 (Pmol/l)	Control	7.32 ± 0.98	6.01 ± 0.96	0.213
	T-test (P-value)	0.007*	0.41	-
	exposure	14.92 ± 1.03	15.31 ± 3.55	0.738
FT_4 (Pmol/l)	Control	13.6 ± 1.75	15.57 ± 2.82	0.511
	T-test (P-value)	0.252	0.824	-

TT_3: total tri iodothyronine, TT_4: total tetra iodothyronine, TSH: thyroid stimulating hormone, FT_3: free tri iodothyronine, FT_4: free tetra iodothyronine, CHE: cholinesterase enzyme, * P-Value<0.05, ** P-Value<0.01

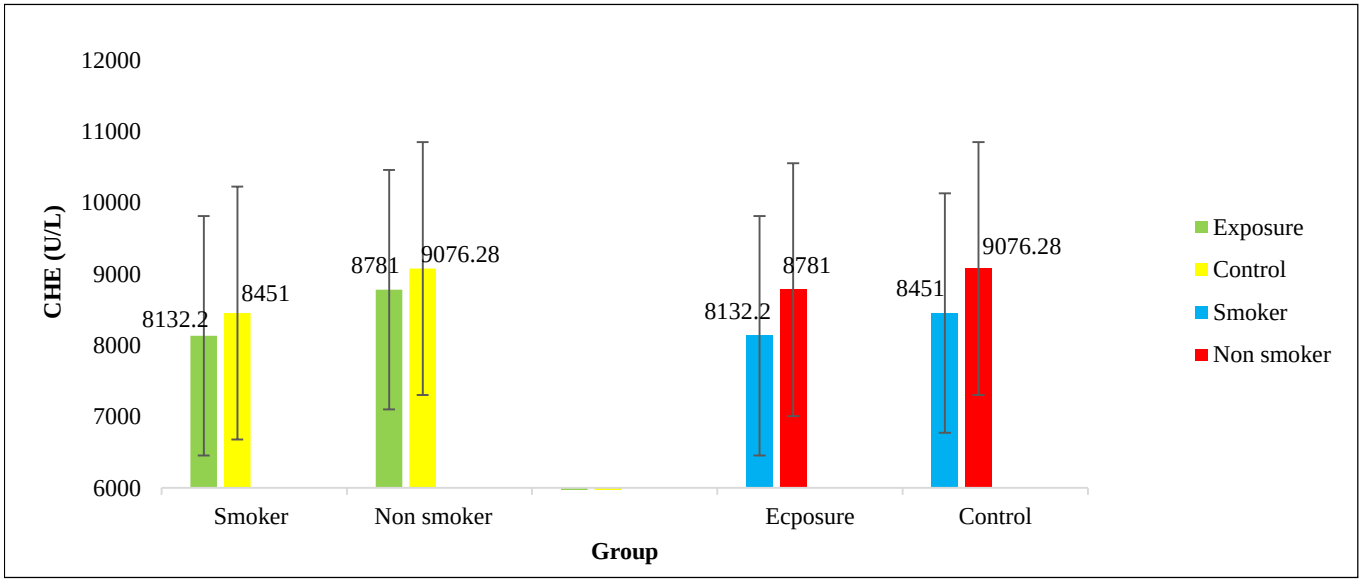

Figure 1. The mean activity of cholinesterase in terms of smoking (p>0.05).
CHE: cholinesterase enzyme

difference was observed regarding the activity of thyroid hormones between the exposure and control groups [21]. The results obtained from the study by Contreras et al. indicated that the level of activity of thyroid and thyroid stimulating hormones did not decline significantly compared to the control among the farmers of Davila state in Venezuela [22], which was in accordance with the present study. In a study by Piccoli et al. on farmers in the southern Brazil, similar to this study, the level of activity of thyroid and thyroid stimulating hormones was normal among the most male and female farmers [23]. In the study by Abou El-Magd et al. on the workers of a factory producing Pyrethroid insecticides, unlike the present study, a significant difference was observed in the level of activity of thyroid and thyroid stimulating hormones

between the exposure and control groups [24]. In the mentioned study, the mean activity of T_3, T_4, and TSH was 1.6±0.21, 6.4±0.92, and 3.38±0.72 respectively in the exposure group, and 2.77±0.53, 8.42±1.4, and 2.42±1.35 respectively in the control group [24]. The most important reason of this difference is related to the fact that in the study by El-Magd et al. both male and female participants were present, and the mentioned factory produced Pyrethroid insecticides [24]. However, only males participated in the present study and the factory produced organophosphorus pesticides. Taha Abdullah Al-shanti et al. [17] Abeer Araf et al. [25] and Bernieri et al. [26] indicated that unlike the present study, a significant increase was observed in the TSH activity along with a significant reduction in the activity of T_3 and T_4 among farmers compared to the control group. In the study by Farokhi et al. on male spray applicators in several villages in Mazandaran province, the activity of TSH hormone increased significantly, while that of T_3 and T_4 diminished significantly in the exposure group compared to the control [18], which was in contrast to the present study. The main reason of discrepancy between the results of the present study and the four others already mentioned studies is that farmers and spray applicators are exposed to organophosphorus toxicants cross-sectionally and seasonally (not constantly), while working in farms causes exposure to other pollutants such as the cereals and barley dust. Further, in the three studies of Taha Abdullah Al-shanti [17] Abeer Araf [25] and Farokhi [18] the biomarker of exposure to organophosphorus pesticides (cholinesterase enzyme) along with FT_3 and FT_4 had not been monitored. In the study by Munoz et al. on male plant breeders in two states in Mexico, the results showed that the level of TSH and T_4 decreased significantly in rainy and cold seasons (high exposure), compared to dry and sunny seasons (low exposure) [27]. One of the most important reasons of incongruence between the results of the present study and the mentioned findings is that plant breeders are exposed to different types of greenhouse gases and chemicals (around 127 types of substances) [28]. Further, in the mentioned study, the biomarker of exposure to organophosphorus pesticides (cholinesterase enzyme) as well as FT_3 and FT_4 hormones had not been monitored.

In investigating previous studies in terms of CHE enzyme activity, the present study was in line with the studies of Ngowi [29] Shadnia [30] and Miranda Adad [31]. However, the results were incongruent with those of Vevien [32] Aroonvilairat [33] Ebrahimzadeh [34] and Selverio [35]. The major reason of discrepancy is associated with the studied population. In the three mentioned studies, the studied population consisted of farmers, while the present study was conducted on workers in a production factory. The studies performed by Abdollahi et al. [36] and Nikoukar et al. [37] unlike the present study, indicated a significant reduction in the mean activity of cholinesterase in the exposure group compared to the control. The two mentioned studies had been performed experimentally on rats with exposure to malathion, while the present study was a field study and the studied population was exposed to a mixture of several organophosphorus pesticides [36, 37].

Based on the results of the present study, there was no significant correlation between the activity of all studied hormones and CHE enzyme. In a study by Dilshad Khan et al. on cotton farmers in cotton pickers and spray applicators, they found that in the cotton picker group, there was a significant correlation between the activity of FT_4 and cholinesterase [38]. However, as with the present study, no significant correlation existed between the activity of CHE and other studied hormones in the groups [38]. Generally, the central nervous system (neurotransmitters such as acetylcholine) is one of the ways for controlling the release of hormones from endocrine glands [11, 13]. Based on this result, it seems that the assumption of the study suggesting that thyroid disorders may occur through inhibiting CHE or accumulation of acetylcholine, i.e. through an indirect mechanism (regulation of the release of hormones through neurotransmitters) is of less importance.

According to the results of the present study, the mean activity of FT_3 diminished significantly in the exposure group compared to the control among smokers. In spite of T_3 lower concentration compared to T_4, T_3 has a greater biological activity. In addition, the free-form of thyroid hormones (not the bound form) has the active and effective state of these hormones. Therefore, it seems that the changes mentioned in FT_3 are more conspicuous [13]. One of the most important reasons of the lower mean activity of FT_3 in smokers in the exposure group compared to smokers of the control group is attributed to the fact that the smokers in the exposure group, are exposed to both organophosphorus pesticides and to the chemical constituents of cigarette including cyanide, nicotine, and thiocyanate [39]. In a study performed by Amal Saad Hussein on workers of an industrial factory producing paint in Egypt, smoking was found as the most important influential factor for T_3 activity [40]. The results obtained from the Zaidi et al. study revealed that age and smoking did not affect T_4 and TSH [20].

LIMITATIONS

The main limitation of the present study is that the studied factory did not have the necessary coordination with the research team for air monitoring; However, the biomarker of exposure to organophosphorus pesticides (cholinesterase enzyme) was measured.

CONCLUSION

In the present study, the mean activity of thyroid and thyroid stimulating hormones had minor changes in the exposure group compared to control. In a limited number of workers, the activity of TT_3 and TSH exceeded the normal range. Further, none of the workers had below normal CHE activity. In other words, no considerable difference and effect was observed in the mean activity of hormones and enzyme studied between the exposure and control groups. Overall, it can be stated that in the present study the workers employed in the factory producing organophosphorus did not develop thyroid disorders and poisoning with organophosphorus toxicants.

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Legend:

TT_3: total tri iodothyronine, TT_4: total tetra iodothyronine, TSH: thyroid stimulating hormone, FT_3: free tri iodothyronine, FT_4: free tetra iodothyronine, CHE: cholinesterase enzyme, a: independent sample T-test, b: one-way ANOVA, r: Correlation, * P-Value<0.05, ** P-Value<0.01

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