Pyrethroid Toxic Effects on some Hormonal Profile and Biochemical Markers among Workers in Pyrethroid Insecticides Company

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Abstract: Background: As Pyrethroids use is common and likely increasing worldwide, so more researches are needed to know its hazardous effects.

Objectives: This study was designed to evaluate chronic toxic effects of synthetic pyrethroids on some hormonal profile (testosterone, estrogen, progesterone & thyroid hormones), respiratory system, liver and kidney functions, in addition, trying to clarify some underlying mechanisms of toxicity through measuring total antioxidant capacity, lipid peroxidation markers (malondialdhyde), and IgE among workers exposed to pyrethroids.

Subjects and Methods: The study included eighteen workers of both sexes exposed to pyrethroids in pyrethroid Insecticides Company. Twenty non exposed workers from the administrative workers of Faculty of Medicine Zagazig University were selected as a control group. All participating workers were interviewed using a pre-composed questionnaire, furthermore they were examined clinically and investigated by measuring some blood parameters as testosterone, estrogen, progesterone, thyroid hormones (T_3, T_4 and TSH), IgE, ALT, AST, creatinine, urea, total-antioxidants and malondialdehyde according to standard procedures.

Results: The studied groups were matched as regard gender, age, duration of work, marital status, income, residence and smoking habit. There was a highly significant prevalence of headache, cough & wheeze among exposed workers compared to control group ($p< 0.001$). Moreover, the exposed group had significantly lower values of testosterone, T_3, T_4, and pan-antioxidants, as compared to control group ($p<0.001$). Also, there was a higher significant values of TSH, IgE, ALT, AST and malondialdehyde among exposed workers as compared to control group ($p<0.001$).

Conclusion & Recommendations: Chronic exposure to pyrethroid insecticides may cause endocrine disrupting effects, respiratory problems, liver function impairment, beside oxidative stress and lipid peroxidation. So we recommended, improving working condition. Restriction of unlimited use of pyrethroid insecticides especially at home and agricultural purposes. Further researches are needed to evaluate pyrethroids effect on large sample to obtain detailed information about the exposure route, pathways, other mechanisms of toxicity and other health hazards.

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1. Introduction

Pesticides are chemical substances that are used for the destruction of environmental organisms which are detrimental to people (Page, 1998).
Pesticide poisoning is an important cause of morbidity and mortality in developing countries. Every year there are 3 million cases of severe poisoning and 220,000 deaths; the majority of these poisonings and 99% of the resulting deaths occur in the third world (Tinoco and Halperin, 1998).

Pyrethroid pesticides are synthetic analogues of pyrethrins, which are natural chemicals found in chrysanthemum flowers. Although synthetic pyrethroids are based on the chemical structure and biological activity of the pyrethrins, the development of synthetic pyrethroids has involved extensive chemical modifications that make these compounds more toxic and less degradable in the environment (U.S. EPA, 2006*a*.&b).

While the use of pyrethroid insecticides has been documented since 1970s, preliminary evidence suggests that usage has been increasing and the pyrethroid insecticides are replacing the organophosphorus insecticides for residential control

(Jose, et al 2010). So the number of human exposures to organophosphorus insecticides decreased, while exposures to pyretheroid insecticides increased (Sudakine, 2006).

Diet is a primary route of exposure to pyrethroids among non-occupationally exposed individuals, particularly food containing pyrethroid residues e.g, vegetables and fruits (ATSDR, 2003). A high proportion of household dust samples contain pyrethroid residues, suggesting that the home environment may also comprise a major exposure source (Colt et al., 2004). Thus, exposure to pyrethroid insecticides is likely to be multi-media and multi-route, as occupational exposure to pesticides occurs also in the manufacturing process during preparation, transport, and application of these products. Exposure occurs among mixers, loaders, and applicators working in fields, greenhouses, parks, and among farm workers (Hernandez-Valero et al. , 2001). As the exposure to synthetic pyrethroids are extensive, animals exhibited changes in their physiological activities beside other pathological features, so the toxicity of pyrethroid insecticides to mammalian animals has received much attention in recent years (Sakr, 2003). Reproductive toxicity, endocrine disruption, neurodevelopmental toxicity and adverse immune system effects related to pyrethroids exposure have been reported in numerous studies (Wang et al., 2009).

Oxidative stress is a harmful process that can mediate damage to cell structures, including lipids, proteins, RNA and DNA which leads to a number of diseases (Saikat, 2010). Environmental agents, such as pesticides, initiate free radical generation that causes different complications in the body (Langseth, 1996).

Several biological defence mechanisms against intracellular oxidative stress are presented in the organism such as antioxidant enzymes (superoxide dismutase, catalase, glutathione reductase and glutathione transferase) and non-enzymatic antioxidants such as carotenoids, vitamin E, vitamin C and glutathione, can also act to overcome the oxidative stress of the pesticides (Evants and Halliwell, 2001).

This study was planned to evaluate chronic toxic effects of synthetic pyrethroids on some hormonal profile { testosterone, estrogen, progesterone & thyroid hormones, triiodothyronine (T_3) and thyroxine (T_4) and thyroid stimulating hormone (TSH) }, respiratory system, liver and kidney functions in addition, trying to clarify some underlying mechanisms of toxicity through measuring total-antioxidant capacity, lipid peroxidation markers (malondialdhyde), and IgE .

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2. Subjects and Methods:

Study design and setting

This comparative cross-sectional study was conducted from October 2009 to January 2010 at family company that makes leading global household pyrethroid insecticides products like:

* Baygon, its active ingredients, (Imiprothrine + Cyfluthrine) which is used as mosquitoes and cockroaches, multi-insect killer. This product is for export purpose.

*Raid and Baygon, their active ingredients (Imiprothrine + Deltamethrine) which are used as cockroaches and ant killer.

*Raid, its active ingredients (D-allethrine + Tetramethrine), which is used as flying insect killer.

* The company makes also other products like (Pledge, Mr Muscle, Shout, Glead and Windox). This company is at Al-Khanka district, Egypt.

Industrial process and exposure:

At preparation section a 500 kilograms of kerosene is withdrawn and heated till 45°C and then the active ingredient Tetramethrin is added and well mixed till complete solubility. Serdox, which is a non active material had added to increase particle size to allow aerosol properties. At the aerosol line the rest of kerosene has been withdrawn to tanks and synergic material is added. Emulsifier as span 80 is added, and lastly the active ingredient D-allethrine is added with continuous mixing and vigorous pouring till complete homogenicity. Finally, examination and supervision of the end product to be ready for commercial use and availability of wide varieties of brands and products.

N.B: Active ingredient for creeping insects (Imiprothrine , Deltamethrine) and for flying insects (D-allethrine ,Tetramethrine and Cyfluthrine).

System of work at the company:

The total number of persons in this company is 53 workers [39 workers (22males & 17 females), 7 technicians , 6 supervisors and the manager] . They work for 8 hours daily, starting from 8 AM to 12 PM in two daily shifts for 5days per week.

Subjects

Eighteen exposed and twenty control workers were agreeing to participate in this study, they are apparently healthy.

Exposed group:

- Eighteen exposed workers from both sexes are included in this study. Six males in the preparation section and twelve (Six males & six females) at the aerosol line section, they were selected according to the following inclusion criteria:

1) No previous (before joining the job) occupational or second job exposure to any type of insecticides.

2) Regular and direct exposure to pyrethroid insecticides emissions for at least three years.

Fig.1: Preparation section

Fig.2: aerosol line section

Control group:
Twenty workers were selected as non exposed control group from the administrative workers of Faculty of Medicine Zagazig University were included in this study according to the following criteria:
1- No previous occupational exposure to pyrethroid insecticides emissions.
2- Matching to the exposed group regarding age, gender, residence, socioeconomic standard, marital status, smoking habit, and duration of work.

* Exclusion criteria for both of the studied groups were
1-Free from viral hepatitis or liver cirrhosis.
2- No history of thyroid disease.
3- No history of drug therapy.
4- Not exposed to ionizing radiation in the last six months.
5- No current infections or cancer (at the time of the study).

Methods
Questionnaire
At first, the study protocol was approved by the *Ethics Committee of Faculty of Medicine, Zagazig University*, then after obtaining permissions from the manager of the company and written informed consents from all the participants, they were asked to fill out a pre-composed questionnaire and interviewed. A personal, occupational and past histories were taken to determine whether they have any medical or endocrinal problems, duration of work (at least 3 years), use of protective measures were also assessed.

Symptoms:
Identification of symptoms of exposure to pyrethroids as headache, cough & wheeze, dyspnea and repeated viral infection were reported according to *Ray and Fry, (2006)*.

2-Clinical examination: General and local examinations of both studied groups were carried out to detect any abnormalities.

3-Laboratory investigations:
*Samples collection:
A sample of 10cc venous blood was withdrawn from each worker under complete aseptic conditions. Blood samples were collected in test tubes remained to clot, centrifuged for obtaining serum samples then, kept at –20^{o}C until they were used to determine the following:
1- Estimation of serum testosterone, estrogen and progesterone levels (ng/ml):

Testosterone, estrogen and progesterone were assayed in serum samples by the use of Roche Elecsys reagent kit (Roche Diagnostica USA) and Modular analyzer used for assay *(Monath et al., 1995& Lu et al., 1999)*.

2- Estimation of serum T3, T4, and TSH: They were measured at Elecsys auto analyzer by Chem - iluminescence method according to *Grughn et al., (1987).*

3-Estimation of total immunoglobulins E (IgE): It was measured using enzyme linked immunosorbent assay (ELISA). Kits supplied by Clinotch Diagnostics and Pharmaceuticals, inc. *(Kulczyski, 1981).*

4- Liver function tests:

Aspartate transaminase and alanine transaminase activities (AST and ALT) were measured using spectrophotometer at a wave length (546 nm) according to Bergmeyer et al., (1978).

5- Kidney function tests:

Creatinine and Urea levels were measured using spectrophotometer a wave length (520 and 578 nm) respectively, according to Patton and Crouch, (1977) & Henry et al., (1974) respectively.

6- Determination of total antioxidant capacity: Total antioxidant capacity, new analytical test that may provide more relevant biological information compared to that obtained by the measurement of individual components as it represents the cumulative effects of all antioxidants either enzymatic or non-enzymatic, present in plasma and body fluids. It was measured using the Spectrophotometer at a wave length (500-510 nm) according to Koracevic and Koracevic (2001).

7- Determination of serum malondialdehyde (MDA): It was measured using the Spectrophotometer at a wave length (535nm) according to *Yoshioka et al., (1997).*

Statistical analysis:

The data were analyzed using the Statistical Package for Social Sciences (SPSS) version 10 software. Quantitative data were compared using student's t test and qualitative data were compared using chi-square (X^2) test or Fisher exact tests. Correlation test used to measure the relationship between quantitative variable. Results were considered significant when p-value < 0.05 (Norusis, 1997).

3. Results:

General and occupational characteristics:

The results of this study showed that there were no statistically significant differences between the studied exposed and the control groups as regard gender, age, duration of work, marital status, income, residence and smoking habit ($p>0.05$). It was found that majority of exposed workers participating in this study were at the aerosol line (66.67%), and half of them were using protective measures (table1).

* Prevalence of symptoms among the studied groups (table 2):

This study reveals that there was a highly significant prevalence of headache, dry irritative cough and wheeze among exposed workers compared to control group ($p<0.001$). Dyspnea and repeated viral infections showed no significant difference between the studied groups ($p>0.05$).

Blood parameters among the studied group:

Table (3) demonstrates that the exposed group had significantly lower values of testosterone, T_3, T_4, and total-antioxidants compared to the control group ($p<0.001$). Moreover, there was a higher statistically significant values of TSH, ALT, AST, IgE, and malondialdehyde (MDH) among exposed group compared to control group. ($p<0.001$).

It was found also that there were no significant difference between the studied groups as regard estrogen, progesterone, creatinine and urea ($p>0.05$). On comparing blood parameters of the exposed workers in preparation section to those in aerosol line section, it was found that AST was significantly higher in workers of preparation section than those of aerosol section (table 4).

Correlation between all studied parameters and duration of work among exposed group:

This study showed no correlation between all studied parameters and duration of work except for total-antioxidants which showed significant negative correlation with duration of work, which means decrement in total antioxidant with the increase in duration of work, Table (4).

Table (1): Comparison of general and occupational characteristics among the studied groups by Chi Squared and Fisher Exact tests.

Characteristics	Exposed workers n = 18	Control group n = 20	P
Gender			
• Male (N. %)	12 (66.67 %)	11 (55%)	0.46
•Female (N %)	6 (33.33 %)	9 (45%)	
Age (year) (X± SD)	36.29 ± 10.9	37.30 ±7.9	0.72
Duration of work (year) (X± SD)	13.38 ± 901	11.80 ± 6.7	0.50
Marital			
• Married	12 (66.67%)	12 (60%)	0.67
• Not Married	6 (33.33%)	8 (40%)	
*Income			
• Sufficient	16 (88.89%)	18 (90%)	1.00
• Not Sufficient	2 (11.11%)	2 (10%)	
Residence			
• Rural	11 (61.11%)	11 (55%)	0.7
• Urban	7 (38.89%)	9 (45%)	
*Smoking habit			
• Yes	2 (11.11%)	2 (10%)	1.00
• No	16 (88.89%)	18 (90%)	
Use of protective measures			
• Yes	9 (50%)		
• No	9 (50%)		
Work section			
• Preparation	6 (33.33%)		
• aerosol line	12 (66.67%)		

P: Non Significant * : Fisher Exact

Table (2): Comparison of prevalence of symptoms among the studied groups by Fisher Exact test.

Symptoms	Exposed workers	Control group	P
Headache			
• Yes	10 (55.56 %)	2 (10%)	
• No	8 (44.44 %)	18 (90%)	0.002*
Cough & Wheeze			
• Yes	6 (33.33 %)	1 (5%)	
• No	12 (66.67 %)	19 (95%)	0.0002*
Dyspnea			
• Yes	4 (22.22 %)	2 (10 %)	
• No	14 (77.78 %)	18 (90 %)	1.06
Repeated viral infections			
• Yes	3 (16.67 %)	1 (5 %)	
• No	15 (83.33 %)	9 (95 %)	0.24

***: p < o.oo1 highly significant**

Table (3): Comparison of blood parameters measurements in the studied groups by (t)test .

Blood Parameters	Exposed workers n = 18	Control group n=20	P
Testosterone (ng/ml) (♂ only)	16.97 ± 4.83 (n=12)	24.91 ± 3.72 (n=11)	0. 001*
Estrogen (Pg/ml) (♀ only)	105 ± 42.50 (n=6)	111 ± 59.44 (n=9)	0.48
Progesterone (Pg/ml) (♀ only)	2.17 ± 1.08 (n=6)	1.71 ± 0.47 (n=9)	0.11
T3 (mmol/L)	1.6 ± 0.21	2.77 ± 0.53	0.001*
T4 (mmol/L)	66.39 ± 9.2	84.25 ± 13.71	0.001*
TSH (ulU/ml)	3.38 ± 0.72	2.42 ± 1.35	0.001*
ALT (U/L)	23.61 ± 7.20	8.15 ± 1.95	0.001*
AST (U/L)	19.61 ± 6.47	12.15 ± 3.06	0.001*
Creatinine (mg/dl)	0.92 ± 0.24	0.75 ± 0.34	0.079
Urea (mg/dl)	30.05 ± 7.32	26 ± 4.95	0.091
IgE ((IU/ml))	158.35 ± 11.33	70.35 ± 20.45	0.0001*
Total- antioxidants (mU/L)	0.35 ± 0.24	1.37 ± 0.45	0.001*
Malondialdehyde (umol/ml)	28.20 ± 22.83	3.49 ± 1.01	0.001*

*** : p < o.oo1 highly significant**

Table (4): Comparison of blood parameters measurements in preparation section and aerosol line section by (t)test .

Blood Parameters	preparation section n = 6	aerosol section n=12	P
Testosterone (ng/ml) (♂ only)	15.98 ± 3.52 (n=6)	18.16 ± 6.29 (n=6)	0.48
T3 (mmol/L)	1.57 ± 0.15	1.62 ± 0.23	0.64
T4 (mmol/L)	64.66 ± 9.3	67.25 ± 9.42	0.58
TSH (ulU/ml)	4.23 ± 0.73	3.70 ± 0.68	0.15
ALT (U/L)	27.0 ± 4.77	21.91 ± 7.77	0.16
AST (U/L)	24.16 ± 3.86	17.33 ± 6.40	0.03*
Creatinine (mg/dl)	0.85 ± 0.32	0.96 ± 0.20	0.36
Urea (mg/dl)	29.16 ± 6.49	30.50 ± 7.93	0.72
IgE ((IU/ml))	152.70 ± 11.39	161.17 ± 10.64	0.13
Total- antioxidants (mU/L)	0.43 ± 0.19	0.31 ± 0.26	0.36
Malondialdehyde (umol/ml)	39.46 ± 31.21	22.57 ± 16.10	0.14

***: p < o.05 significant**

Table (5): Correlation between total- antioxidants (mU/L)and duration of work (year) in the exposed group.

	Total- antioxidants (mU/L)	
	r	P
Duration of work (year)	-0.49	0.036*

***: p < o.05 significant**

4. Discussion:

Insecticides are the chemicals widely used in agriculture, environmental health, human-and animal-health fields. Exposure to insecticides has been associated with many hazardous effects *(Kanbur et al., 2008).* The widespread use of pyrethroids and the corresponding increase in human exposure have led to toxicological interest *(Kolaczinski and Curtis, 2004).* Several studies have proven that pyrethroids are endocrine disrupting insecticides (EDs). An "endocrine disrupting chemical" is best defined as "an exogenous substance that causes adverse health effects in an intact organism, or its progeny, secondary to changes in endocrine function *(EEC, 1996).* Many of the endocrine disrupting pesticides are active *in vivo* at extremely low doses which can be made by the permitted residue levels in food *(Weltje et al., 2005)* or exposure to low levels of EDs, the effects of which can be additive *(Soto et al., 1994).* Testosterone levels and sperm counts in men have reportedly declined during the last 20 years *(Travison* et al*., 2007).* Low testosterone levels have been shown to contribute to low bone and muscle mass, impaired sexual function, and decreased fertility (Thomas et al., 2008).

Environmental chemicals are suspected of playing a role in these declines *(Swan* et al*., 2003).* Synthetic pyrethroid insecticides are among the most commonly used chemicals today *(John et al., 2009).*

The results of the present study demonstrated that serum testosterone levels is significantly lower in pyrethroid exposed workers compared to the control group, these findings are in accordance with *Zhang et al., (2007)* who stated that the widely-used synthetic insecticide Permethrin dramatically reduces testosterone levels and sperm counts in adult male mice. Another study in non-occupationally exposed men, reported statistically significant relationships between pyrethroid insecticide metabolite concentrations and circulating testosterone hormone levels. They attributed these findings to the increased use of pyrethroid pesticides that results in widespread exposure among the general population (*John et al., 2009).*

The results of the present study could be explained by *Melissa et al., (2007)* Who reported that pyrethroids as a class of non-steroidal compounds, can interact competitively with human androgen receptors and sex hormone binding globulin, and suggest a mechanism by which chronic exposure to pyrethroid may result in disturbances in endocrine effects relating to androgen action, as it may exert estrogenic and/or anti-androgenic activity. The same findings were reported before by *Eil and Nisula, (1990)* when pyretheroid compounds (Pyrethrins and Bioalletherine) were tested in human genital skin fibroblasts.

Zhang et al., (2007) found that Permethrin causes reproductive damage by altering the beginning steps of testosterone synthesis in the mice testes that leading to lowering testosterone production in the testes and blood.

In the current study, there was no significant difference between exposed and control groups as regard serum estrogen and progesterone, as Pyrethroids-induced estrogen disrupting effects didn't interfere with serum estrogen hormone levels. For example, Cypermethrin, Deltamethrin and their metabolites (3-phenoxybenzoic alcohol & 3-phenoxy benzoic acid) exhibited significant estrogenic activities comparable to 17B-estradiol (E_2) when they were evaluated for their estrogenic activities in the MCF-7 human breast carcinoma cell line *(Jin et al., 2010).*

Synthetic pyrethroids referred to as xenoestrogens which are a diverse group of substances that do not necessarily share any structural resemblance to the natural hormone 17B-estradiol (E_2). However, they may exert oestrogenic effects by mimicking or inhibiting the action of endogenous estrogens by their ability of binding to the estrogen receptors, and therefore inducing or attenuating a response *(Kojima et al., 2004).*

In this work, the pyrethroid exposed workers had a significantly lower triiodothyronine (T_3) and thyroxine (T_4) serum levels as well as a significantly higher thyroid stimulating hormone (TSH) serum levels when compared to control group.

Our results are in a accordance with *Akhtar et al., (1996), Maiti and Kar, (1998), Wang et al., (2002) and Finch et al., (2006)* who found decreased serum levels of both T_3 and T_4 and increased serum levels of TSH in experimental rats exposed to different synthetic pyretheroid compounds.

Maiti and Kar, (1998), has explained that there is also decrease in the activity of hepatic type I iodothyronin 5´-monodeiodinase (5´ D-I) which is one of the deiodinase enzymes that convert T_4 to the more potent T_3 with consequent decrease in T_3 and elevation in TSH serum levels.

Moreover, *Finch et al., (2006) have* otherwise attributed the increase of TSH levels to pyrethroid induced increase in hepatic microsomal thyroxine UDP glucuronosyl transferase activity which leads to increased glucuronidation and elimination of thyroxine. Consequently, a compensatory increase in pituitary gland production of TSH, and also increase in thyroid gland production of thyroid hormones should occur to keep up with the elimination.

Finch et al., (2006) added that this is the same mechanism underlying pyrethrins – induced rat thyroid gland tumors as the trophic effects of TSH occurs in the form of increased thyroid gland weight, follicular cell hypertrophy and replicative DNA synthesis. Thus, Pyrethrin-induced thyroid gland tumors are similar to that of some other non-genotoxic inducers of hepatic xenobiotic metabolism.

The results of the present study revealed that the exposed workers complain of some respiratory symptoms like cough, wheeze, shortness of breath and dyspnea. These symptoms coincide with increase in IgE level, when compared with the control group.

The results of the present study pass in parallel with *He et al., (1998),* who stated that there is some evidence that pyrethroid compounds are sensitizers in human populations.

Clinical studies involving insecticide-sensitive patients with asthma have suggested that some asthmatics have declines in lung function due to exposure to insecticide aerosols containing Permethrins (Salome et al. , 2000).

Other occupational and agricultural studies have reported positive associations between Permethrin pesticide exposure and wheeze or asthma in adults *(Hoppin et al., 2006 & 2008).*

Reardon et al., (2009) reported that higher pre-natal levels of *Cis*-permethrin were associated with early cough, wheeze, and IgE production. .

Martinez et al., (1995), explained that early wheeze can be transient and attributed to viral infections, whereas persistent wheeze is more likely to have an underlying allergic component.

In this study there was a significant increase in the serum levels of aspartate transaminase (AST) and alanine transaminase (ALT) in the pyrethroid exposed workers as compared to control group.

These findings coincide with Al-sarar et al., (2009) who reported a slight elevation in AST, ALT and ALP serum levels in pesticides-exposed workers of Riyadh municipality, KSA. Significant increase in the levels of these enzymes, which is also positively correlated with pesticide residues, were found in occupationally exposed tobacco farmers in Pakistan *(Khan et al., 2008).* The increase in the level of ALT and/or AST is a good indicator of hepatic toxicity *(Hall, 2001).*

Recent experimental studies have shown that Lambda-Cyhalothrin increases the enzymatic activities of aminotransferases AST and ALT, which is ameliorated with co-administration of vitamin C *(Fetoui et al., 2010).* Cypermethrin, a synthetic pyrethroid insecticide, have been shown to increase liver enzymes and produce necrosis of hepatocytes cytoplasmic vaculation, bile duct hyperplasia and mononuclear cellular infiltration in the liver of broiler chicks which is ameliorated by combination of Vitamin E and selenium *(Aslam et al., 2010).*

The results of this work revealed normal kidney function (urea & creatinine) in exposed worker.

These findings coincide with *Al-Sarar et al., (2009)* who found insignificant elevation in urea and creatinine among pesticide sprayer in Riyadh ,who exposed to both pyretheroid and organophosphorus , and with *Satpathy et al. ,(1997)* who found no toxic effects on renal function among adult males after short-term exposure to Cyfluthrin.

In contrast to our findings, two laboratory studies showed that male kidneys of mice and rats may be particularly susceptible to synthetic pyrethroid (Sumithrin) (Cox, 2003). In our opinion the conflict with our findings may be due to route of exposure as animals in those studies were fed Sumithrin for two generations.

Normal kidney functions reported in our study means that kidney functions is still good and compensated, our opinion explained before by Feinfeld, (1998) who found that at least 50% of kidney function must be lost before the rise of serum creatinine could be detected.

The results of the present work revealed a significant decrease in total antioxidant capacity of exposed workers in addition, a significant increases in malondialdehyde (MDH) level, compared to the control group.

The results of the present study pass parallel with *Vontas et al., (2001), Cinzia et al., (2004), Sadowska et al., (2010)* ,Who stated that pyrethroid exposure associated with oxidative stress, as it induced lipid peroxidation , protein oxidation and depleted multiple antioxidant enzymes like, reduced glutathione , glutathione peroxidase, catalase and superoxide dismutase activities.

Kanbur et al., (2008) found that, the degree of oxidative stress and lipid peroxidation induced by pyrethroid, related to the dose administered, the duration of exposure and the administration of the indicated compounds, either alone or as a combination.

A predominance of reactive oxygen species (ROS) production and DNA damage can contribute to cytotoxicity of Cis-bifenthrin (synthetic pyretheroid insecticide), *Wang, et al., (2009).* The depletion in total antioxidant capacity as well as the increment in MDH (lipid peroxidation marker) could be explained by *Banerjee et al., (2001)* who suggested that the formation of oxygen free radical can be a major factor in the toxicity of pesticides. On the other hand, *Nasuti et al (2003) and Prsanthi et al., (2005)* reported that oxidative damage, induced by pyrethroids might be

due to their lipophilieity, whereby they could penetrate easily to the cell membrane and caused membrane lipid peroxidation.

5. Conclusion:

Despite of being the least toxic pesticides, pyrethroids still have a harmful effects, as chronic exposure to pyrethroids can cause endocrine disrupting effects, liver function impairment and respiratory problems. Oxidative stress, lipid peroxidation and allergy may be some underlying mechanisms of toxicity.

Although workers in preparation section are considered more exposed to pyrethroids than those in aerosol line section, there was no significant differences between them in the studied hormonal and biochemical parameters except for AST enzyme. This may be attributed to wearing of the protective clothes (specialized overalls, gloves and shoes) specially during the preparation process, however they neglect wearing masks.

Recommendations:

As there are worldwide exposure to Pyrethroids which may be environmental, occupational or at home so we recommended the following :

Improving working conditions and following hygienic measures, beside supplementation of antioxidants to workers to overcome oxidative stress.

Restriction of unlimited use of pyrethroid insecticides especially at home or for agricultural purposes .

Periodic examination of Pyrethroids exposed workers both clinically and laboratory for early detection of any abnormalities.

Further researches are needed to evaluate pyrethroids effect on large samples to obtain detailed information about the exposure route, pathways, metabolites, other mechanisms of toxicity, and other health hazards.

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