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NEUROBEHAVIORAL AND MENSTRUAL DISORDERS AMONG ADOLESCENT FEMALES ENVIRONMENTALLY EXPOSED TO PESTICIDES, MENOUFIA GOVERNORATE, EGYPT

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Abstract

Introduction: Adolescent females living in agricultural areas where crops are routinely sprayed by pesticides are expected to be environmentally exposed to pesticides´ health hazards partially as those occupationally exposed. **Aim of work**: to assess neurobehavioral and menstrual disorders among adolescent females environmentally exposed to pesticides. **Materials and methods:** This was a cross-sectional study conducted on 100 pesticide exposed adolescent females who had one or more of family members are pesticides´ seasonal applicators and 50 non- exposed adolescent females matched for age and education, served as controls at Menoufia governorate, Egypt; during the period of pesticide application season of cotton crop from the first of May to the end of September 2017. A self-administered questionnaire and a series of neurobehavioral tests were administered and serum acetyl cholinesterase (AChE) activity was assessed. **Results:** A significant lower AChE activity levels were detected among the exposed group compared to the controls (Mean±SD=238.49± 23.83 vs 303.35±78.54 IU/L; respectively). There were significant higher mean scores of trail making test (parts 1 and 2) and significant lower mean scores of (similarities test, Benton visual retention test, block design test, Santa Ana dexterity test (dominant and non-dominant hands) and Beery visuo-motor imitation test among the exposed group compared to the controls ($P<0.05$). Also, the exposed group reported more prevalent irregular menstrual cycle (26.8%) and intermenstrual bleeding (28.2%) compared to the control participants (8.1% and 8.1%; respectively). **Conclusion and recommendations**: Adolescent females living in agricultural areas and from families whose one or more members are pesticides´ applicators had significantly lower neurobehavioral performance, report more prevalent menstrual irregularities and have lower levels of serum AChE compared to the control group. The neurobehavioral deficits demonstrated a dose–response relationship with AChE levels among the exposed participants. This necessitates the need for implementation of health education programs to prevent or reduce health effects associated with pesticide exposure to adolescent females.

Key words: Environmental pesticides ‘exposure, Adolescent females, AChE ,Menstrual and Neurobehavioral disorders.

Introduction

Pesticides are toxic chemicals that are widely used throughout the world in agriculture on crops as well as for domestic purposes; for mosquito and cockroach control operations (Rani et al., 2017). Organophosphate pesticides (OPs) represent a class of pesticides with high toxicity and are used in both farmlands and households (Zhu et al., 2015). The pesticide exposure of farmers’ families, especially children, can be potentially significant as there is a combination of para-occupational, environmental and domestic exposures (Silvério et al., 2017). Residential exposure depends on proximity of the house to areas treated with pesticides, the persistence of pesticides used in or around the home and domestic uses at home on pets (flies and ticks) and also on humans (lice and scabies) (Bouvier et al., 2005; Mamane et al., 2015). Direct exposure to pesticides can occur during the application whereas indirect exposure of farm spouses and children to pesticides can occur through spray drift, transfer of contaminated dust and soil from treated fields to farm vehicles and buildings. Also, handling contaminated clothes and personal contacts of exposed individuals by any member of the family may track pesticides indoors on their clothes, shoes, skin and hair (El-Sebae, 1993; Lee et al., 2015). In addition, indirect exposures can occur through non-target species as air, water and soil and they represent routes of long-term low-level exposures. Pesticide use raises a number of environmental concerns. Over 98% of sprayed insecticides and 95% of herbicides reach a destination other than their target species (Miller, 2004). According to the Egyptian culture ; no females are recruited in pesticides′ application, hence their exposure to pesticides could be exclusively environmental either by living nearby agriculture fields, domestic use as home pesticides, or to pesticides′ residues spoiling clothes or skin and/or hair of their family members (brothers or fathers) working as pesticides′ applicators. Pesticide exposure can cause a variety of adverse health effects ranging from simple irritation of the skin and eyes to more severe effects such as endocrine disruption, blood and neurobehavioral disorders as well as the possibility of an increased risk of cancer especially, childhood cancers such as Non-Hodgkin lymphoma and leukemia (Clayton et al., 2003; Mamane et al., 2015). Organophosphate pesticides exposure can result in some neurobehavioral disorders such as memory loss, loss of coordination, reduced speed of response to stimuli, reduced visual ability, altered or uncontrollable mood; general behavior and reduced motor skills (Silvério et al., 2017). Menstrual disorders like longer, irregular and missed menstrual cycles in addition to intermenstrual bleeding were detected among females exposed to carbamates and / or OPs compared to women who never used pesticides (Farr et al. 2004). Pesticides are thought to pose a considerably higher risk to children than to adults as they are more vulnerable due to the significant anatomical and maturational physiological changes occurring in the brain during developmental periods including adolescence (Abdel-Rasoul et al., 2008). Most evidence for health effects of pesticides in adults comes from studies of occupationally exposed males. Relatively less is known about pesticide-related health effects in females, and there may be sex-specific risk differences with respect to reproductive toxicity. In addition, comparatively little is known about non-occupational pesticide exposure pathways (Rohlman et al., 2007).

Aim of work

This study aims to assess neurobehavioral and menstrual disorders among adolescent females environmentally exposed to pesticides.

Materials and methods

Study design: This was a cross-sectional study.

Place and duration of the study: The study was conducted at three randomly chosen districts (Shebin El-Kom, El-Bagour and Menouf) out of ten districts at Menoufia governorate. The pesticide exposed female adolescents' homes lie within less than 1000 meters from the agricultural fields. The study conducted during the period of pesticide application season of cotton crop from the first of May to the end of September 2017.

Study sample: Out of 123 single adolescents female (aged from 9-18 years) whose one or more of their family members were pesticides′ seasonal applicators at cotton fields and / or working privately with their own backpack sprayers for other crops all over the year in the three selected districts, one hundred (81%) were eligible for inclusion in this study. About 19% were excluded due to either of refusal to participate in the study or weren't fulfill the inclusion criteria.

World Health Organization has stated adolescent age from 10-19 years (WHO, 2015). In the present study we considered the age start from 9 years to cover all ages of menarche in Egyptian girls (Abdel Hameed, 2017).

The control group included 50 adolescent females that were matched with the exposed group regarding age, residence, socioeconomic standard, educational level and their families were never involved in field pesticides´ applications. Their homes lied by more than 1000 meters away from the agricultural fields. All the chosen female adolescents in both groups were single.

Exclusion criteria included history of chronic medical disorders (diabetes, hypertension, asthma, thyroid disease, liver or kidney disease, peripheral neuropathy, vitamin deficiency) and illiteracy.

Study methods: each participant was subjected to the following:

I: A predesigned questionnaire which included:

a. Personal data as age, residence, level of education, income, distance of house from fields and past medical history of diseases.
b. Menstrual history as age of menarche, regularity of cycles, intermenstrual bleeding.
c. Pesticide exposure history as applying pesticides at home, use of empty pesticide container for different purposes, handling contaminated clothes of their relatives, existing in the fields within 3 days after pesticide spraying.
d. Occupational history of their pesticide applicators' relatives: working days and duration of work.
e. Neurological symptoms as headache, dizziness, blurred vision, impaired memory and concentration.

II: Clinical examination*:* general examination including anthropometric measures (weight, height and body mass index) and neurological examination.

III: Neurobehavioral test batteries which included:

Age appropriate versions of the Wechsler Adult Intelligence Scale (WAIS) that were validated in an Arabic speaking population were used to assess neurobehavioral function for the studied participants. Better performance is evaluated by higher scores obtained on tests of Information, Similarities, Arithmetic, Digit Symbol, Block Design, Digit Span, and the Benton Visual Retention Test. In contrast, lower latencies or time to complete Trail Making A and B indicate better performance. Examiners were blind to the status of the participant as exposed or control (Misdraji et al., 2010).

IV: Serum acetylcholine esterase (AChE) assessment:

Five milliliters of blood were drawn from all participants and serum AChE was determined according to Weber (1966) using standard kits (Test-combination Boehringer Mannheim GmbH Diagnostica). Serum AChE was selected because it is a better short-term indicator of cholinesterase inhibition than red blood corpuscles (RBCs) AChE due to its more rapid response to exposure; it is used as an indicator of recent, acute exposure to cholinesterase inhibiting pesticides. Also, because the primary pesticide being applied is chlorpyrifos, which has a preferentially inhibiting effect on serum AChE rather than RBCs AChE (Gotoh et al., 2001).

Consent

Written informed consents were signed by all participants before being enrolled into the study.

Ethical approval

Medical Ethics Committee at Menoufia Faculty of Medicine approved the study protocol.

Data management

Data were analyzed using IBM SPSS version 22 (SPSS Inc., Chicago, Illinois, USA). Chi- squared test (χ^2) was used to examine the relation between qualitative variables. Z test is a significance test for testing proportions. For quantitative data, comparison between two groups was done using student t-test. Pearson correlation coefficient test was used to study the correlation between two quantitative variables. P values less than 0.05 were considered statistically significant.

Results

There was non-significant difference between exposed and control groups regarding socio-demographic data (age, income and education level), body mass index (BMI), past clinical history ($p>0.05$) (data weren't illustrated in tables).

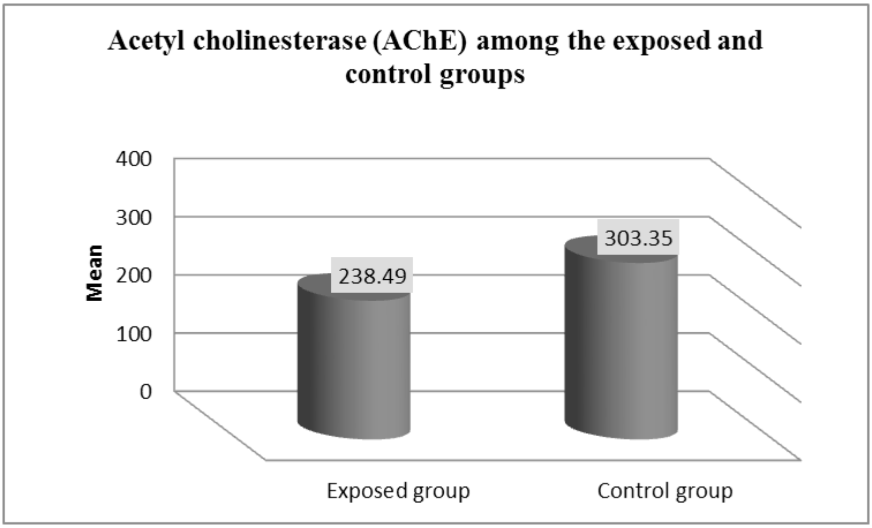

Figure 1: Mean levels of serum AChE among exposed and control groups

A lower activity levels of AChE was found among the exposed compared to the control group (Mean± SD =238.49± 23.83 versus 303.35 ±78.54 IU/L; P < 0.001) as shown in figure (1).

Table (1): Prevalence of neurological manifestations among the studied groups.

Neurological manifestations	Studied groups				Z test	p value
	Exposed (No=100)		Controls (No =50)			
	No	%	No	%		
Dizziness	30	30.0	6	12.0	2.23	**0.02***
Headache	18	18.0	4	8.0	1.39	0.16
Blurred vision	27	27.0	4	8.0	2.50	**0.01***
Difficulty in concentration	24	24.0	5	10.0	1.83	**0.03***
Impaired memory	27	27.0	3	6.0	2.81	**0.004****
Feeling depressed	26	26.0	1	2.0	3.38	**0.003****
Feeling anxious	17	17.0	4	8.0	1.25	0.21
Insomnia	11	11.0	2	4.0	1.13	0.25
Fatigue	31	31.0	3	6.0	3.24	**0.001****
Numbness	13	13.0	5	10.0	0.27	0.78
Twitches, or involuntary movements in limbs	7	7.0	0	0.0	1.51	**0.04***

*: Statistically significant **: Highly statistically significant

Table 1 showed that there was a statistically significant higher prevalence of dizziness, blurred vision, difficulty in concentration, impaired memory, feelings of depression, fatigue and involuntary movements in limbs among the exposed group compared to controls.

Table (2): Mean ± SD of neurobehavioral performance among the studied groups.

Neurobehavioral tests	Studied groups		t-test	p value
	Exposed (No=100)	Controls (No =50)		
Attention: Trail making test part 1	89.60±16.44	81.70±18.11	2.58	**0.008***
Trail making test part 2	176.35±39.27	158.55±39.52	2.61	**0.009***
Concentration: Similarities test	10.31±2.59	13.91±3.11	7.50	**<0.001****
Intellectual function: Block design test	28.94±3.06	31.55±2.37	5.29	**0.004***
Visual perception and memory: Benton visual retention test	5.70±1.66	6.87±2.07	3.39	**0.007***
Hand dexterity: Santa Ana dexterity test (dominant hand)	40.49±2.58	46.31±2.91	12.47	**<0.001****
Santa Ana dexterity test (non-dominant hand)	37.78±3.57	39.82±3.12	3.44	**0.007***
Visuo-motor integration: Beery visuo-motor imitation test	12.96±2.17	15.13±1.09	6.66	**0.002***

*: Statistically significant **: Highly statistically significant

Table 2 showed that there was a statistically significant higher mean scores of trail making test (parts 1 and 2) among the exposed group compared to the controls and a statistically significant lower mean scores of (similarities test, Benton visual retention test, block design test, Santa Ana dexterity test (dominant and non-dominant hands) and Beery visuo-motor imitation test ($p<0.05$).

Table (3): Correlations between neurobehavioral tests' performance with AChE activity levels, duration of work of pesticide applicator family member among the exposed group.

Neurobehavioral tests	**Exposed group (No =100)**		
	Days worked in the current season	**Worked years**	**AChE (IU/l)**
	r	**r**	**r**
Attention: Trail making test part 1	**0.19***	**0.21***	**-0.31***
Trail making test part 2	**0.35***	**0.63***	**-0.22***
Concentration: Similarities test	**-0.28***	**-0.39***	**0.33***
Intellectual function: Block design test	-0.25	-0.14	0.03
Visual perception and memory: Benton visual retention test	-0.04	-0.12	0.12
Hand dexterity: Santa Ana dexterity test (dominant hand)	**-0.44***	**-0.41***	**0.61***
Santa Ana dexterity test (non-dominant hand)	**-0.39***	**-0.42***	**0.43***
Visio-motor integration: Beery visio-motor imitation test	**-0.33***	**-0.47***	**0.55 ***

r=Pearson correlation coefficient *: Statistically significant

Table 3 showed that there was a statistically significant positive correlation between AChE activity levels and duration of exposure with tests of Similarities, Santa Ana dexterity test (dominant and non- dominant hand) and Beery visio-motor imitation. On the other hand, there was a statistically significant negative correlation between AChE activity levels with Trail making tests (part 1 and part 2).

Table (4): Menstrual history among the studied groups.

Menstrual history	Studied groups				χ^2 test	p value
	Exposed (No =100)		Controls (No =50)			
	No	%	No	%		
Menarche:						
Yes	71	71.0	37	74.0	0.15	0.69
NO	29	29.0	13	26.0		
Menarche age	No =71		No =37		t-test = 1.64	0.11
	12.97±1.88		12.35±1.82			
Menstrual cycle:						
Regular	52	73.2	34	91.9	5.22	**0.02***
Irregular	19	26.8	3	8.1		
Intermenstrual bleeding:						
Present	20	28.2	3	8.1	4.70	**0.03***
Absent	51	71.8	34	91.9		

*: Statistically significant **: Highly statistically significant

Table 4 showed that the exposed group had a statistically significant higher prevalence of irregular menstruation and inter-menstrual bleeding compared to the control group.

Discussion

This study revealed an evidence for environmental exposure to pesticide among adolescent females living in agricultural areas and with one or more of their relatives who were working as pesticide applicators. It is critical to study pesticide-related health effects and reducing pesticide exposures in this group.

Acetyl choline esterase (AChE) level was used as a biomarker for exposure to OP pesticides (Knudsen and Hansen, 2007). The present study found a significant lower level of AChE among exposed compared to controls (Fig 1). This result was consistent with many previous studies from different countries (Jørs et al., 2006; Lu, 2007; Khan et al., 2010) that reported significant associations between exposure to pesticides and cholinesterase inhibition among farm workers.

The pesticide exposed adolescent females also reported significant higher prevalence of various neurological symptoms as dizziness , blurred vision , difficulty in concentration , trouble in remembering, feelings of depression , irritability , fatigue , twitches and involuntary movements of arms or legs compared to the control participants (Table 1). The relationship between exposure to pyrethroid compounds and prevalence of neurological symptoms as dizziness (Walters et al., 2009) blurred vision, headache and fatigue (Sutton et al., 2007) and muscle tremors (Ismail et al., 2018) has been reported by many studies.

Our study showed that there was a significant association between the exposure to pesticides and decrement in neurobehavioral performance for attention, concentration, intellectual function, visual perception and memory and visio-motor coordination ($p<0.05$, Table 2). These results were in accordance with two previous Egyptian studies done by Rohlman et al., 2014; Rohlman et al., 2016 on organophosphorus pesticide exposure and neurobehavioral performance among adolescents in Egypt.

Also our study revealed the presence of a statistically significant negative correlation between the number of days worked by pesticide applicator family members at the current season and years worked as pesticide applicators with test of concentration (Similarities) and tests of visuomotor coordination (Santa Ana dexterity test dominant hand and Beery visio-motor imitation) subtests and by significant positive correlation with tests of attention (Trail Making 1 and 2). Moreover, the significant correlation between AChE activity level and the same tests (Table 3). These findings were similar to the results of Roldan-Tapia et al., 2005, in their work on neuropsychological effects of long-term exposure to organophosphate pesticides indicated by inhibition of AChE and reported a significant relationship between the period of exposure on applying OP pesticides, performance deficits and increased prevalence of neurological manifestations. Exposed adolescent females showed a significantly higher prevalence of menstrual disturbances than controls from the same communities (Table 4). These results were in agreement with the findings obtained by Farr et al. (2004) who found that women who worked with pesticides had a 60–100% increased odds of experiencing long cycles, missed periods, and intermenstrual bleeding compared with women who had never worked with pesticides. Also, Cooper et al. (2005) reported that exposure to particular pesticides as polychlorinated biphenyls (PCBs) can affect the menstrual cycle and may induce ovarian dysfunction. Moreover, some previous studies done by Abell et al. 2000 and Idrovo et al., 2005 on time to pregnancy among female greenhouse workers, they detected that exposure to pesticides in female workers in flower greenhouses may have implicated in reduced their fertility.

Exposure to pesticides has been associated with menstrual cycle disturbances most probably due to potential effects of endocrine disrupting pesticides on the female reproductive system as modulation of hormone concentrations, ovarian cycle irregularities and impaired fertility (Bretveld et al., 2006).

Conclusion and recommendations

Adolescent females living in agricultural areas and from families whose one or more members are pesticides´ sprayers have significantly lower neurobehavioral performance, report more prevalent neurological manifestations and menstrual irregularities and have lower activity levels of serum AChE compared to the control group. The neurobehavioral deficits demonstrated a dose–response relationship with AChE levels among the exposed participants. This necessitates the need for implementation of health education programs to prevent or reduce health effects associated with pesticide exposure to adolescent females.

Limitations of the study: This study had several limitations. First, it was a cross sectional study design, so we were unable to derive any conclusions on the causality of pesticide exposure and neurobehavioral or menstrual effects in adolescent females. Second, the small sample size might limit this study to be generalized. Therefore, these results should be verified with large-scale and cohort studies.

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Conflict of interest

None declared.

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