هفدهمین کنفرانس سراسری و پنجمین کنفرانس بین المللی زیست شناسی ایران

Neurocognitive impairment and Mental health status in farmers exposed to organophosphate pesticides

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Abstract
The aim of this study was to study toxicity of organophosphate (OP) pesticides in exposed farmers in terms of neurocognitive impairment, mental health status. A comparative cross-sectional analysis was done in 174 farmers who had been exposed to OPs in comparison to a control group containing 174 healthy subjects with the same age and sex and education level. The neurocognitive impairment and psychological disorders were significantly raised in workers. The present findings indicate that inhibition of AChE can be incidence of neuropsychological disorders.

Keywords: Organophosphate, Neurocognitive impairment, Mental health status

Introduction

The latest estimate by a WHO task group indicates that there may be 1 million serious unintentional poisonings each year and in addition 2 million people hospitalized for suicide attempts with pesticides. This necessarily reflects only a fraction of the real problem. On the basis of a survey of self-reported minor poisoning carried out in the Asian region, it is estimated that there could be as many as 25 million agricultural workers in the developing world suffering an episode of poisoning each year (Jeyaratnam , 1990).Anticholinesterase compounds,organophosphates(OPs)and carbamates (CMs) are commonly used for a variety of purposes in agriculture and in human and veterinary medicine. They exert their toxicity in mammalian system primarily by virtue of acetylcholinesterase (AChE) inhibition at the synapses and neuromuscular junctions, leading into the signs of hypercholinergic preponderance. However, the mechanism(s) involved in brain/muscle damage appear to be linked with alteration in antioxidant and the scavenging system leading to free radical-mediated injury(Milatovic,2006).Careless use of pesticides like organophosphate (OP) insecticides may causes diverse health complications by up setting the nervous, endocrine, reproductive, and immune systems (Soltaninejad,2009). WHO approximation is that around one million severe unintentional and two million intentional poisoning with insecticides come about worldwide, and of these almost 220,000 die (WHO, 1997).The health effects of acute exposure to pesticides are characterized very well but the long-term health effects among exposing people after a chronic low-level exposure is under question.

Study population

A relative cross-sectional study with a total number of 374(252 male,122 female) subjects was accomplished. All subjects gave informed consent before the beginning of the study and the approval of the study protocol by the Institute Review Committee. The first cohort included 187 horticulture farmers, with age range of 16-80, who worked as farmers. Control subjects were selected from the same village consisting of 187 workers who were not engaged in any agricultural work and had no history of job-related exposure to OP pesticides. Information on working history, socioeconomic status (salary, education), and lifestyle information (smoking, alcohol consumption, drug uses, consumption of vitamin or antioxidant supplements, and dietary habits) were achieved by a questionnaires completed in a conversation between the subject and an expert examiner. Mental health status evaluated by General Health Questionnaire (GHQ-28) (Moritz,2004; Goldbeg and Williams, 1988). All subjects were submitted to comprehensive clinical examination to identify any signs or symptoms of long-lasting illnesses such as arterial hypertension, heart failure, cancer, thyroid disturbance, asthma, diabetes, and anemia. Those with chronic disease, alcohol consumption, antioxidant consumption, and/or under drug usage, or contact to poisonous materials, radiation therapy, or substance abuse were left out from the study.

Subjective Neurocognition Inventory (SNI)

The self-report questionnaire consists of 76 items with a focus on everyday memory and attention problems. Part of the questionnaire is the “Fragebogen Erlebter Defizite der Aufmerksamkeit” (FEDA, Questionnaire for the measurement of self-experienced deficits of attention), a questionnaire that taps attentional difficulties (Zimmermann,1991).This scale was complemented by new items constructed by Moritz et al. Items had to be endorsed on a five-point likert scale (very frequently-never).The following domains were tested: selective attention (10 items), divided attention (4 items), long-term memory (7 items),

prospective memory (7 items) and psychomotor retardation (9 items). One item tapped the forgetting of names (for a more through description (Moritz,2004).General Health Questionnaire (GHQ-28) The Iranian version of the General Health Questionnaire (GHQ28) was used to identify high risk subjects for mental disorder, as well as the following four symptoms: "somatic symptoms", "anxiety and insomnia", "social dysfunction", and "severe depression"(Goldbeg , 1988).

Statistical analysis

Multivariate analyze variance were used for statistical comparisons after plotting and testing for equal variances. Pearson correlation coefficient was used to study the association between variables. All data are presented as mean+SD.PValues lower than0.05 were considered statistically significant.

Results

Table 1 shows the average levels of subjects ages, years of employment, smoking habits (years and N/day), and sex. There was no statistically significant difference between two groups in terms of age and years of employment but smoking habits significantly different in workers and controls.

Table 2 shows that Psychomotor Speed (PS), Selective Attention (SA), Divided Attention (DA), Verbal Memory (VM), Nonverbal Memory (NVM), Prospective Memory (PM), Spatial Functioning (SF) and Initiative/Energy (I/E) were significantly decreased in workers as compared with controls.

Table 1. Summary of demographic data in workers and control subjects

Subjects	Farmers (n= 174)	Controls (n= 174)	p Value
Age (years)	37.94±12. 41	37.05±11.78	0.48
Sex	126(Male) 61(Female)	126 (Male) 61(Female)	-
Work history (year)	9.78±7. 72	-	
Smoking (years)	0.39 ±2.45	1.36±5.3	0.026
Smoking (N/day)	0.62±3.75	1.07±4.1	0.27

Data represent mean ± SD.

Table 2. The status of Neurocognitive impairment in controls and workers

Group	PS	SA	DA	VM	NVM	PN	SF	IE	Total
Farmer	23.68±6.31	29.47±7.77	14.2955±4.89	26.55±7.34	14.44±4.87	23.49±5.75	14.16±5.68	35.90±9.78	247.57±47.25
Control	31.15±3.16	43.34±5.49	17.98±3.20	34.58±4.26	17.70±2.78	30.84±3.6	18.24±4.84	47.11±6.73	332.40±32.15
df	1	1	1	1	1	1	1	1	1
F	98.60	187.29	34.92	78.95	29.79	102.98	26.32	78.59	193.93
PValue	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001	0.0001

VM: verbal memory; NVM: nonverbal PS: psychomotor speed; SA: selective attention; DA: divided attention; memory; PM: prospective memory; SF: spatial functioning; and I/E: initiative/energy

Data represent mean ± SD.

Discussion

The results of this study show that Neurocognitive impairment and psychological disorders were significantly raised in workers.As the first thought, it can be said that exposure to OP pesticides in the farmers has resulted in the production of free radicals and oxidative stress.In support, there are some study reporting increasing association between low levels of pesticide exposure and deficits in neurobehavioral performance(Rothlein,2006). Another study reported that Exposure to low levels of pesticides over many years of agricultural work is associated with neurological impairment as measured by the Selective Attention,Symbol-Digit, Reaction Time tests. Experience handling pesticides was also associated with deficits in neurobehavioral performance (Rohlman ,2007). Another work provides powerful evidence in favor of a causal relationship between OP exposure and significant neuropsychiatric disorder including mood

destabilization and CI (Davies,2000).Actually, most of studies reported previously indicate incidence of neuropsychological disorders in occupationally OP-exposed workers (Fiedler,1997).It seems that large toxic doses of organophosphorus compounds cause acute necrotic neuronal cell death in the brain, whereas sublethal or subclinical doses produce apoptotic neuronal cell death and involve oxidative stress and on the other hands OPs can inhibit the enzyme neuropathy target esterase and acylpeptide hydrolase and these are causes for neurocognitive disorders.

Reference

Davies R, Ahmed G, Freer T (2000) Chronic exposure to organophosphates: background and clinical picture. Advances in Psychiatric Treatment 6: 187–192.

,Kipen H,Kelly-McNeil K,et al.(**1997**) **Fiedler N** Long-term use of organophosphates and neuropsychological performance. American Journal of Industrial Medicine 32(5):487-96.

Goldbeg D, Williams PA. A user's guide to the GHQ. Windsor: NEFR-Nelson, **1988**

J. Acute pesticide poisoning: a major **Jeyaratnam** global health problem. World Health Stat Q. **1990**;43(3):139-44.

Milatovic D , Gupta RC, Aschner M (2006) Anticholinesterase Toxicity and Oxidative Stress. The Scientific World Journal 6: 295-310.

Moritz S, Ferahli S, Naber D. Memory and attention performance in psychiatric patientslack of correspondence between clinician-rated and patient-rated functioning with neuropsychological test results. Journal of the International Neuropsychological Society, 10 (**2004**), pp. 623–633.

, Lasarev M, Anger WK, Scherer Rohlman DS J, Stupfel J, McCauley L. Neurobehavioral performance of adult and adolescent agricultural workers. Neurotoxicology. 2007 Mar;28(2):374-80. Epub **2007** Dec 4

, Rohlman D, Lasarev M, Phillips J, Rothlein J Muniz J, McCauley L. Organophosphate pesticide exposure and neurobehavioral performance in agricultural and non-agricultural Hispanic workers. Environ Health Perspect. **2006** May;114(5):691-6

Soltaninejad K, Abdollahi M (2009) Current opinion on the science of organophosphate pesticides and toxic stress: A systematic review. Medical Science Monitor 15(3): 75-90.

WHO,1997.Guidelines for poison control. WHO in collaboration with UNEP and ILO,Geneva,pp.3-10.

Zimmermann P, Messner C, Poser U, Sedelmeier P . Ein Fragebogen erlebter Defizite der Aufmerksamkeit (FEDA) [a questionnaire measuring self-experienced deficits of attention]. Psychologisches Institut der Universität Freiburg, Freiburg (Germany) **(1999)**