هفدهمین کنفرانس سراسری و پنجمین کنفرانس بین المللی زیست شناسی ایران

Biochemical toxicity biomarkers in farmers exposed to organophosphate pesticides Results

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Abstract
The aim of this study was to study toxicity of organophosphate (OP) pesticides in exposed farmers in terms diabetes and hematological factors. 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 levels of fasting blood glucose, blood urea nitrogen(BUN), cholesterol, triglycerides, creatiniine, high-density lipoprotein (HDL), aspartate aminotransferase (AST) and alanine aminotransferase (ALT) and alkaline phosphates (ALKp) were measured in the blood of the subjects. The mean level of Fasting blood glucose, BUN, cholesterol and ALT was significantly raised in workers while Creatinine, triglycerides and Alkalin phosphatase significantly decreased as compared with controls. The mean levels of AST and Fbs2 in the workers and controls were not statistically different. The present findings indicate that inhibition of AChE can be incidence of a risk for prediabetes. Use of supplementary antioxidants would be useful in the treatment of farmers.

Keywords: Organophosphate, Diabetes,toxicity

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). In both type 1 and type 2 diabetes, diabetic complications in target organs arise from chronic elevations of glucose. The pathogenic effect of high glucose, possibly in concert with fatty acids, is mediated to a significant extent via increased production of reactive oxygen species (ROS) and reactive nitrogen species (RNS) and subsequent oxidative stress (Evans, 2003). 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 pathogenesis of type 2 diabetes is complex, with two distinct mechanisms: insulin resistance (decrease of insulin action on peripheral tissues) and insulin deficiency (impaired insulin secretion by pancreatic beta-cells). These abnormalities are due to genetic and environmental factors (Pinget ,2002;Rezg,2010). The prevalence of diabetes for all age-groups worldwide was estimated to be 2.8% in 2000 and 4.4% in 2030. The total number of people with diabetes is projected to rise from 171 million in 2000 to 366 million in 2030(Wild, 2004). Many studies provides support that POP exposure might contribute to type 2 diabetes mellitus (Abdollahi ,2004; Turyk , 2009; Ukropec,2010; Rignell-Hydbom ,2009; Ruckmani ,2011; Codru , 2007; Teimouri ,2006; Slotkin, 2011;Hectors, 2011). OPs in chronic toxicity produce free radicals and disturb body oxidant/antioxidant status that results in cell wall damage and cell nuclear toxicity (Ranjbar, 2002 ; Bayrami,2012).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. The first cohort included 187 horticulture farmers, with age range of 16-80, who worked as farmers around a village 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. Blood samples were collected from counted in subjects throughout the course of a spraying season between 7 and 8 AM before arriving the place of work on Saturday as the beginning of the weekly work. The levels of Fasting blood glucose,Urea, cholesterol, triglycerides, cratinin, High-density lipoprotein (HDL), Aspartate aminotransferase (AST) and Alanine aminotransferase (ALT) and alkaline phosphates (ALKp) were measured.

Statistical analysis

All data were analyzed with Stats Direct 2-7-8.Two-sample t test and data. Pearson correlation coefficient was used to study the association between variables. All data are presented as mean+SD. p Values lower than 0.05 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 the average levels of Fasting plasma glucose, Blood urea nitrogen(BUN), cholesterol,triglycerides,Creatinine, High-density lipoprotein (HDL), Aspartate aminotransferase (AST) and Alanine aminotransferase (ALT) and alkaline phosphates (ALKp). The mean level of Fasting blood glucose, Urea, cholesterol and ALT was significantly raised in workers while Creatinine, triglycerides and Alkalin phosphatase significantly decreased as compared with controls. The mean levels of AST and Fbs2 in the workers and controls were not statistically different.

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

Table2. Hematological parameters in controls and workers

Group	Fasting plasma glucose	BUN(mg/dL)	Creatinine(mg/dL)	Cholesterol (mg/dL)	Triglycerides (mg/dL)	HDL (mg/dL)	AST (IU/L)	ALT (IU/L)	ALKp(IU/L)	Oral glucose tolerance test(mg/dL)
Control	76.95± 27.66	28.38± 9.50	.86±. 13	160.27± 32.47	136.78± 92.82	47.03± 10.90	30.82± 10.16	20.02± 8.26	114.23± 43.388	86.29± 24.97
Farmer	84.89± 13.59	30.64± 10.3	.82±. 183	174.50± 43.72	123.59± 53.43	44.85± 7.47	24.26± 10.2	20.19± 13.32	93.14±2 7.78	86.27± 14.48
pVal	0.001	0.027	0.00 01	0.015	0.0001	0.0001	0.49	0.001	0.015	0.99

Discussion

The results of this study show that the level of Fbs, Urea, cholesterol and ALT were significantly higher in the farmers as compared with controls, while the cratinin, triglycerides and Alkalin phosphatase level in workers were lower than controls. 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 interview with farmers, it was found that they did not use proper protection tolls like mask, gloves, long boots, head cover, face cover, and they did not take shower in a regular manner. The only safety tools that they used were a kind of cloth masks.The present findings about increased of Fasting blood glucose is in agreement with the previous studies on workers who were chronically exposed to OP pesticides (Rezg,2007). In rodents it has been demonstrated that small doses of bisphenol-A have profound effects on glucose metabolism. Therefore, this altered blood glucose homeostasis may enhance the development of type 2 diabetes (Alonso-Magdalena ,2010). Another study reported that Several POPs at low doses similar to current exposure levels may increase diabetes risk, possibly through endocrine disruption (Lee, 2010) . Other study reported that Simultaneous exposure to various POPs in the general population may contribute to development of obesity, dyslipidemia, and insulin resistance, common precursors of type 2 diabetes and cardiovascular diseases. Although obesity is a primary cause of these metabolic abnormalities, POPs exposure may contribute to excess adiposity and other features of dysmetabolism (Lee, 2011). Moreover sub chronic malathion exposure causes progressive hyperglycemia which can be a risk factor for diabetes(Ruckmani, 2011).Also Increasing serum concentrations of individual POPs considerably increased prevalence of prediabetes and diabetes in a dose-dependent manner. Interaction of industrial and agricultural pollutants in increasing prevalence of prediabetes or diabetes is likely.Taken together, these findings provide other evidence that OPS has the propensity to impair glucose homeostasis, also may induce diabetes associated with stimulation of hepatic gluconeogenesis and glycogenolysis in favor of glucose release into the blood(Ukropec,2010).

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