Simposium Persatuan Biologi Gunaan Malaysia Ke-11

The 11th Symposium Of The Malaysian Society of Applied Biology

MSAB 2010

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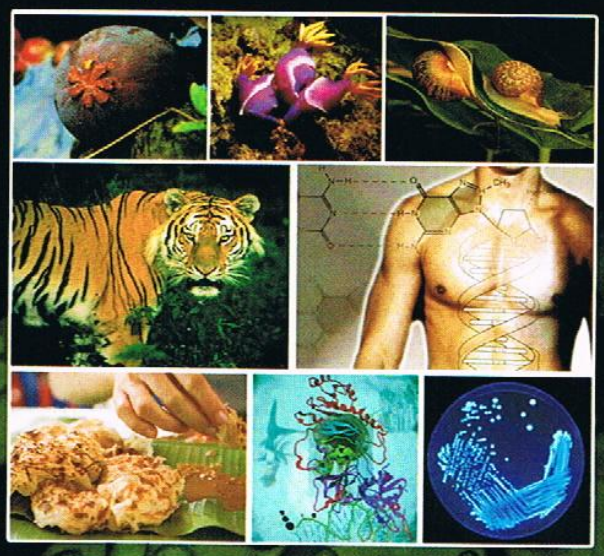

Keseimbangan Biologi Ke Arah Kelestarian Hayat

"Biological Balance Towards Life Sustainability"

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Biological Balance Towards Life Sustainability

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Paraoxonase (PON1) Activities and Lipid Profiles among Organophosphates (OPs) Pesticide Exposed Workers

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ABSTRACT

Paraoxonase (PON1) is high density lipoprotein (HDL)-associated enzyme which is known to hydrolyze organophosphates (OPs) into harmless substances and prevent atherosclerosis by inhibiting oxidative modification of LDL. Reports showed low PON1 activity among OPs exposed individuals, while low PON1 activity was associated with a high risk of coronary artery disease (CAD). The link between OPs exposure and lipid profiles which are known risk factors of CAD has not yet been reported. This study aimed at comparing the activities of PON1 and lipid profiles between workers who are exposed to OPs and non-exposed control groups. A total of 105 subjects (53 OPs exposed and 52 non-exposed) were recruited. Fasting serum samples were analyzed for PON1 activities and lipid profiles. The results showed a significantly lower diazoxonase activity ($p<0.05$) among the OPs exposed group but there were no differences in lipid profiles ($p>0.05$) between the two groups. Our study suggested that the decreased PON1 activity among OPs exposed individuals cannot be linked to atherosclerosis and CAD through lipid profiles. A larger scale study is required to confirm our observation.

Keywords: Paraoxonase, organophosphate, lipid profiles.

INTRODUCTION

Organophosphates (OPs) are the most commonly used pesticides, as they are more effective than other types of pesticides on arthropods and other insects (Davies et al., 2000). In Malaysia, OPs are mainly used in agriculture in order to increase productivity (Department of pesticides control, Ministry of Agriculture Malaysia, 2009). Due to their easy accessibility, OPs poisoning became the second most common poisoning in Malaysia after paraquat (Tara et al., 1989).

In the body, OPs are hydrolyzed by paraoxonase (PON1) into diethylthiophosphate and a 'leaving group' which are relatively non-toxic (Sudakin and Power, 2007). This protects the exposed individuals from their toxic effects. Additionally, PON1 is also the main HDL-related enzyme that hydrolyzes the oxidized low-density lipoprotein (ox-LDL) as well as prevents the accumulation of lipid peroxides on LDL (Mackness et al., 1997; Aviram and La Du, 1998; Aviram et al., 1999; Durrington et al., 2001). This mechanism might give protection against atherosclerosis which is the hallmark of coronary artery disease (CAD).

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In the meantime, PON1 activities were reported to be low among agricultural workers due to exposure to OPs (Hernandez et al., 2003; Mackness et al., 2003; Sozmen et al., 2007; Hofman et al., 2009; Lopez et al., 2009). Growing evidences showed that lack of PON1 was associated with inability to hydrolyze OPs (Li et al., 2000; Mackness et al., 2003; Yeung et al., 2007) and ox-LDL (Shih et al., 1998; Aviram et al., 1999; Navab et al., 2000), thus renders an individual with lack of PON1 to be susceptible to OP toxicity and atherosclerosis. Apart from that, acute OPs exposure has also been shown to induce oxidative stress in human (Ranjbar, et al., 2002) as well as increase the low density lipoprotein cholesterol (LDL-C) and triglycerides (TG) in animals (Lasram et al., 2008). Since elevated TG and LDL-C are among independent risk factors of atherosclerosis (Witztum et al., 1991; Hokanson et al., 1996; Assmann et al., 1999; Sarwar et al., 2007), these findings provided evidences that OPs exposure may play a role in the development of atherosclerosis and CAD. To our knowledge, the link between chronic OPs exposure and lipid profiles in human has not yet been reported. The increasing exposure to OPs and the rising annual mortality due to CAD in Malaysia (National Institute of Health Malaysia, 2006) warrants more researches to be done in this area.

MATERIALS AND METHODS

This is a cross-sectional comparative study. Convenient sampling was used to select the subjects who fulfilled the inclusion and exclusion criteria based on our questionnaire. Fifty three pesticide sprayers from 4 farms in Kuantan, Pahang were recruited and 52 control subjects were selected based on matching process of age, ethnicity and income bracket. Fasting serum samples were analyzed for PON1 activities towards substrates paraoxon, phenylacetate and diazoxon as well as for total cholesterol (TC), TG, high density lipoprotein cholesterol (HDL-C) and LDL-C.

The paraoxonase, arylesterase and diazoxonase activities were determined spectrophotometrically according to methods described by Eckerson et al. (1983), Gan et al. (1990) and Davies et al. (1996) respectively. Enzyme activities were expressed as U/ml. The TC, TG and HDL-C were analyzed by ADVIA 1200 Chemistry System while LDL-C was calculated using Friedewald formula (Friedewald et al., 1972). The lipid profiles were expressed in mmol/l. The parametric data were presented as mean (SD) while the non parametric data were presented as median [interquartile range (IQR)]. The comparison of PON1 activities and the level of lipid profiles between the OPs exposed and the control groups were done by independent t-test (parametric data) and Mann-Whitney U test (non-parametric data).

RESULTS

The demographic data were homogeneous between the OPs exposed and the control groups. There were no significant differences ($p>0.05$) between the two groups with regard to age, race, body mass index (BMI) Kg/m^2 and smoking status. The period of exposure among the OPs exposed subjects ranged from 7-204 months.

The diazoxonase activity was significantly lower in exposed group (Table 1) while the lipid profiles were not significantly different between the two groups (Table 2).

Table 1: Comparison of PON1 activities between the OPs exposed and the control group.

PON1 activities (U/ml)	OPs Exposed Group (*n=53*) Mean (SD)	Control (*n=52*) Mean (SD)	*t*-stat	df	*p*-value
Basal paraoxonase	156.96 (58.87)	176.59 (66.33)	-1.605	103	0.112
Arylesterase	90.06 (17.14)	96.57 (23.89)	-1.606	103	0.111
Diazoxonase	850.93 (206.75)	988.62 (244.11)	13.121	103	0.002*

Independent t-test, results presented as mean (SD)
*significant difference ($p<0.05$) in the mean diazoxonase activity between the exposed and the control groups

Table 2: Comparison of lipid profiles between the OPs exposed and the control group.

Lipid profiles (mmol/l)	OPs Exposed Group (*n=53*) Median (IQR)	Control (*n=52*) Median (IQR)	*t*-stat	df	*p*-value
TC (mmol/l)	5.10 (1.09)	5.36 (1.61)			0.274
TG (mmol/l)	1.15 (0.84)	1.17 (0.68)			0.465
HDL (mmol/l)	1.32 (0.44)	1.33 (0.38)			0.177
LDL (mmol/l)	3.09 (0.86[a]	3.37 (0.95)[a]	-1.554	103	0.123[†]

Mann-Whitney U test, results presented as median (IQR), [a]Mean (S.D), [†]independent t-test

DISCUSSION

Our present study demonstrated lower PON1 activities among the OPs exposed group even though only diazoxonase showed a significant difference ($p<0.05$). This finding is similar to the report by other authors (Mackness et al., 2003; Kuang et al., 2006; Sozmen et al., 2007). The lower PON1 activities among the OPs exposed group may be due to the metabolic activation of OPs to highly toxic oxon as the PON1 can be inactivated by these compounds (Aviram et al, 1999).

Although not statistically significant ($p>0.05$), the lipid profiles were observed to be lower among the OPs exposed group. This is similar to a study by Choudhari and Chakraharti (1984) which reported a decrease HDL-C after OP exposure. As PON1 is HDL-associated enzyme, the lower PON1 activities as observed in this study may be due to the lower HDL-C in the exposed group.

Even though previous study by Lasram (2008) showed an increase in LDL and TG in animals after acute OPs exposure, chronic OPs exposure in human seems to have a reverse result in our study. Our findings were somehow similar to reports by Ibrahim and El-Ghamal (2003)

and Ryhanen et al. (1984) where the TC and LDL-C were lower following an exposure to OPs in animals. TC and LDL reduction was suggested to be due to OPs-induced stimulation of LDL receptors which enhances the clearance of cholesterol from circulation (Brown et al., 1981).

In conclusion, our study suggested that the decreased PON1 activity among OPs exposed individuals cannot be linked to the atherosclerosis and CAD through the lipid profiles. A larger scale study is required to confirm our observation.

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