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ASSOCIATION BETWEEN SELECTED PARAMETERS INVOLVED IN GLUCOSE HOMEOSTASIS AND SEVERITY OF ANTICHOLINESTERASE INSECTICIDE POISONING

T.K.R.R. Senarathne[1], U. Hettiaratchi*[1], S. Siribaddana[2], H. Peiris[1], L. Athiththan[2]
[1]Department of Biochemistry, Faculty of Medical Sciences, University of Sri Jayewardenepura, [2]Department of Medicine, Faculty of Medicine and Allied Sciences, Rajarata University of Sri Lanka.
**Corresponding author (email: usha@sjp.ac.lk)*

Introduction

Organophosphates (OP) and carbamate pesticides are widely used in agriculture as the commonest means of pest control methods especially in developing countries. Poisoning due to pesticides accounts for approximately 3 million cases of hospitalization globally, including 200,000 deaths from OP intoxication per year [1]. Poisoning can be either accidental or intentional. OP act by inhibiting the enzyme acetyl cholinesterase. Symptoms are usually due to muscarinic, nicotinic and central nervous system receptor overstimulation. In addition to those cholinergic manifestations, biochemical changes like glucose dysregulation have also been observed in human and animal studies [2, 3].

Studies have reported altered glucose homeostasis and insulin resistance in acute and chronic exposures to OP, many previous experiments have observed pronounced increase in blood glucose level in parallel with high serum insulin levels as a result of malathion intoxication. The mechanisms involved in the pathophysiology of insulin resistance following OP and carbamate exposure remains under investigations. Some suggested mechanisms include, formation of advanced glycation end products, accumulation of lipid metabolites, activation of inflammatory pathways and oxidative stress.

Many studies have reported that OP impair glucose homeostasis and cause insulin resistance which may lead to the development of type 2 diabetes. Diabetes mellitus has also become an increasing health burden in South Asia with an estimated 82 million affected in 2017 and a predicted population of 151 million in 2045 [2]. Some have suggested exposure to pesticide as one of the contributory factors in the development of diabetes mellitus in agrarian areas. Majority of the supporting evidence are from animal experiments.

Hence, present study was focused to assess the association between selected parameters of glucose homeostasis and the severity of poisoning following intentional ingestion of OP and carbamate insecticide

Materials and Methods

This prospective study was carried out with 100 acute OP and carbamate poisoned patients with age ranging from 18-60 years, presenting within 24 hours of poisoning, admitted to Teaching Hospital Anuradhapura. Proxy consent obtained initially and before discharge informed written consent was taken from the patient. Ethical approval was obtained from ethics review committee of faculty of Medical Sciences, University of Sri Jayewardenepura.

The inclusion criteria of the study was patients diagnosed with OP or carbamate poisoning by the clinician according to standard management protocol (Management of poisoning, Prof. Ravindra Fernando) and patients who are admitted within 24 hours of ingestion. The exclusion criteria were, history of poisoning with other toxic substances other than OP and carbamate, pregnant women, subjects with chronic alcoholism, co-ingestion of alcohol and evidence of chronic diseases (diabetes, liver, renal, pancreatic, malignancies etc.).

Data were collected using interviewer administered questionnaire from guardian and patient. First blood sample (5 mL) was collected on admission for analysis of random blood sugar level (RBS) and glycosylated haemoglobin (HbA1c) level.

Severity of poisoning was measured on admission based on the method given as Peradeniya Organophosphorus Poisoning scale (POP). According to POP scale, 0-3 score were considered as mild poisoning, 4-7 as moderate poisoning and 8-11 as severe poisoning.

Second blood sample (5 mL) was collected at the discharge, following 8 – 10 hours of fasting for the analysis of fasting blood glucose (FBS) and fasting serum insulin. Insulin resistance (IR) was calculated using homeostasis model assessment of insulin resistance equation (HOMA-IR). HOMA-IR = {FSI (µU/mL) × FBG (mmol/mL)}/22.5

HOMA -IR above 2.5 were considered as insulin resistance. Data were analyzed using SPSS version 21.

Results and Discussion

Subjects (100) with normal HbA1c on admission and no evidence of diabetes were recruited and the majority was males (3). The mean age (SD) of the total population was 33±12 years. Among the study population 45 subjects were identified as organophosphate poisoning while 55 were identified as carbamate poisoning**.**

At the time of discharge mean values (±SD) serum insulin, FBS, and IR were 18 ±16 µIU/ mL, 114 ±36 mg/dL, and 5.7+±6.5 respectively. Mean values of all the biomarkers assessed were significantly elevated in moderate poisoned group compared to mild poisoned group. 11 subjects were included in the severe poisoned group and only 3 survived after treatments, thus the values are not included in the table (Table 01).

Table 1. Mean values of assessed biomarkers according to the POP scale

Parameter	Severity of poisoning based on POP scale		
	Mild (64)	Moderate (33)	Significance (P value)
RBS (mg/ dL) *	120 ± 39	170 ± 58	0.000
S. Insulin (µIU/ mL) *	13 ± 10	27 ± 23	0.001
FBS (mg/ dL) *	102 ± 18	127 ± 23	0.000
HOMA IR *	3 ± 2	9 ± 9	0.002

Mean values were significantly different at 0.01 level (p<0.01)

Studies have observed an increase in blood glucose levels in parallel with a high insulin secretion into blood through malathion intoxication supporting the findings of current study [4][5][6].

Several studies have also found that insulin resistance is induced by OP insecticides supporting the findings of the current study [7] [8].
The severity of poisoning significantly correlated with the following biochemical parameters; on admission RBS level, and fasting serum insulin level, FBS, HOMA IR measured at the time of discharge. (Table 02).

Table2. Correlations between assessed parameters and severity of poisoning according to pop scale

Parameter	Pearson's correlation coefficient - r	P value
RBS (mg/ dL)	0.470	0.000
S. Insulin (µIU/ mL)	0.301	0.001
FBS (mg/ dL)	0.516	0.000
HOMA IR	0.393	0.000

Correlations were significant at the 0.01 level (p<0.01)

The elevation of FBS, fasting serum insulin and insulin resistance in these patients could be probably associated with activation of inflammatory pathway and oxidative stress.

Conclusions and recommendations

Severity of OP and carbamate poisoning was associated with hyperglycaeima, increased insulin and insulin resistance. Further studies will be needed to evaluate the underling mechanism of increased IR and it is important to commence follow-up studies to assess the risk of developing Type 2 diabetes and persistent elevation of HOMA-IR.

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