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Research Article

Hepatic and Renal function in Applicators and Farmers Exposed to Organophosphate Pesticides in Southwest, Nigeria

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Abstract

Prolonged exposure to organophosphate pesticides (Op) has been associated with various diseases. There is little information on which group of exposed farm workers that is more affected. This study therefore evaluated indices of hepatic and renal function in pesticide applicators and farmers exposed to organophosphate pesticides. Thirty (30) pesticide applicators (PA), 30 farmers exposed to Op and 30 control subjects were recruited into this study. Serum activity of acetyl cholinesterase (AChE) was determined using HPLC while total bilirubin (TBIL), conjugated bilirubin (CBIL), total protein (TP), albumin, urea and creatinine were determined using standard colorimetric method. Serum activities of alkaline phosphatase (ALP), aspartate aminotransferase (AST), alanine aminotransferase (ALT), gamma-glutamyl transferase (GGT) were determined using Auto analyzer (Hitachi 902). AChE activity, levels of albumin and TP were significantly lower while creatinine and activities of AST, ALT and GGT were significantly higher in PA than in controls. Similarly, AST, ALT and GGT activities were significantly higher while the levels of albumin, TP, urea and AChE activity were significantly lower in farmers than in controls. Remarkably, serum AChE activity and levels of albumin and TP were significantly lower while AST and ALT activities were significantly higher in PA compared with farmers. This study demonstrated that liver and renal dysfunction are associated with organophosphate pesticides exposure but pesticides applicators appear to be at greater risk of having liver dysfunction than the farmers. Farm workers exposed to organophosphate pesticides may benefit from periodic assessment of their liver and renal function for early detection of any possible dysfunction.

Keywords: Farmers, Kidney, Liver, Organophosphate toxicity, Pesticide applicators

INTRODUCTION

Several hundred pesticides have been used in agricultural practice in order to enhance food production. These pesticides differ greatly in their modes of action, uptake by the body, metabolism, elimination from the body and toxicity to humans (Anwar, 1997). Among pesticides, Op has been among the most used, as these compounds are non-persistent in the environment (Simonian et al., 2005). They are frequently used to spray cocao, cashew and mango plantations in South-Western Nigeria which is the tree crop belt of the country, yet they remain an important source of poisoning (Kesavchandran et al., 2006).

Occupational exposure to Op pesticides is usually through skin absorption and inhalation (Keifer et al., 1996). Most previous studies reported that Op exert toxicity on the target and non-target organs through inhibition of acetyl cholinesterase in the nerve and muscle tissues (Mileson *et al*., 1998). Though measurement of serum AChE activity remains the gold standard for monitoring exposure to Op (Misra *et al*., 1994), alteration of hepatocellular function of the liver (being central to metabolism of Op) and induction of subtle renal damage to the kidney (being the route of elimination of Op) have not been extensively examined as target organs of OP toxicity (Rastogi et al., 2009). Most of the farmers and OP applicators are poor and not educated enough to afford and know the importance of assessing Op toxicity. Therefore, there is need for simple and easily affordable parameters to monitor exposure to Op.

Exposure to Op had been previously shown to cause hematological and biochemical disturbances (Kanlender et al., 2005; Yaqub et al., 2013), kidneys, lungs and hepatic damage (Gomes et al., 1999; Owoeye et al., 2012) and increases in transaminases (Frazzetto et al., 2012). These reports suggest that hepatocellular and renal damage may be involved in the toxicity of Op. Although there are available reports on the impact of Op toxicity on the kidney and liver function, there is little information on which group of exposed farm workers at risk of severe toxicity. This present study therefore determined indices of hepatic and renal function in Nigerian Op applicators and farmers exposed to organophosphate pesticides.

MATERIALS AND METHODS

After obtaining informed consent from each subject and an approval from the Joint Ethics Committee of the University

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of Ibadan/University College Hospital (UI/UCH), 60 farm workers (30 Op applicators and 30 farmers) aged 47±17 years and 30 controls aged 46±10 years were recruited into this study. The control group consisted of apparently healthy subjects who are not occupationally exposed to Op. Serum activity of AChE was assayed using HPLC. Serum bilirubin was estimated by photometric method based on the diazo reaction, total protein by Biuret method, albumin by dye binding method, urea by Diacetylmonoxime method and creatinine by Jaffe's alkaline picrate method. Activities of ALP, AST, ALT and GGT were determined using Auto analyzer (Hitachi 902). Briefly, Hitachi 902 is an automated biochemistry analyzer which uses spectrophotometric method to process biological fluid specimens. Differences in means of the variables were determined using the Student's t-test while the relationship between all the variables was determined using Pearson's correlation. *P*-values less than 0.05 were considered significant

RESULTS

Table 1 shows the mean serum AChE activity and indices of hepatic and renal function in PA and Op exposed farmers compared with controls. Mean serum activity of AChE and levels of albumin and TP were significantly lower while serum creatinine and mean activities of AST, ALT and GGT were significantly higher in PA compared with the control(P = 0.000, 0.000, 0.000, 0.027, 0.000, 0.000, 0.000 respectively). Similarly, mean activities of AST, ALT and GGT were significantly higher while levels of albumin, TP, urea and mean activity of AChE were significantly lower in farmers compared with the control subjects (P = 0.000, 0.000, 0.044, 0.000, 0.000, 0.000, 0.023 respectively).

Table 1:
AChE activity and indices of hepatic and renal function in pesticides applicators (PA), farmers and controls.

Controls (n=30)	Pesticides Applicators	Farmers (n=30)	Indices (n=30)
AChE (IU/ml)	9.38±0.82	6.63±0.90*#	7.88±0.63*
TBIL (mg/dl)	0.61±0.02	0.68±0.03	0.67±0.02
CBIL (mg/dl)	0.21±0.01	0.24±0.02	0.21±0.01
ALP (IU/L)	84.77±7.60	84.33±9.71	84.80±8.90
AST (IU/L)	22.07±4.46	34.20±5.42*#	30.17±5.70*
ALT (IU/L)	17.60±4.86	29.50±4.76*#	25.37±4.14*
GGT (IU/L)	26.70±9.02	42.93±13.92*	44.03±8.70*
Albumin (g/L)	3.77±0.39	2.93±0.58*#	3.32±0.39*
TP(g/L)	8.13±0.47	7.45±0.62*#	7.84±0.60*
Urea (mg/dl)	24.73±8.89	22.07±9.26	20.13±6.14*
Creatinine (mg/dl)	0.66±0.18	0.76±0.16*	0.72±0.18

**Significantly different from controls, #significantly different from farmers, AChE=acetyl cholinesterase, TBIL=total bilirubin, CBIL=conjugated bilirubin, ALP=alkaline phosphatase, AST=aspartate aminotransferase, ALT=alanine aminotransferase, GGT=gamma-glutamyl transferase, TP=total protein*

Table 2:
Correlation of AChE activity with indices of hepatic and renal functions in pesticides applicators

Indices	r-value	p-value
Total Bilirubin (mg/dl)	-0.16	0.398
Conjugated Bilirubin (mg/dl)	-0.04	0.844
ALP IU/l)	-0.14	0.464
AST (IU/l)	-0.17	0.360
ALT (IU/l)	0.10	0.619
GGT (IU/l)	-0.04	0.826
Albumin (g/L)	0.13	0.499
Total protein (g/L)	-0.14	0.451
Urea (mg/dl)	-0.07	0.711
Creatinine	0.05	0.805

AChE=acetyl cholinesterase, TBIL=total bilirubin, CBIL=conjugated bilirubin, ALP=alkaline phosphatase, AST=aspartate aminotransferase, ALT=alanine aminotransferase, GGT=gamma-glutamyl transferase, TP=total protein

Table 3:
Correlation of AChE with hepatic and renal profiles in farmers exposed to organophosphate pesticides

Indices	r-value	p-value
Total Bilirubin (mg/dl)	-0.38	0.040*
Conjug. Bilirubin (mg/dl)	-0.34	0.066
ALP (IU/l)	-0.02	0.927
AST (IU/l)	0.30	0.108
ALT (IU/l)	0.05	0.782
GGT (IU/l)	0.19	0.319
Albumin (g/l)	-0.19	0.313
Total protein (g/l)	-0.11	0.549
Urea (mg/dl)	0.06	0.739
Creatinine (mg/dl)	0.15	0.433

#Significant at $P<0.05$ (2-tailed), AChE=acetyl cholinesterase, TBIL=total bilirubin, CBIL=conjugated bilirubin, ALP=alkaline phosphatase, AST=aspartate aminotransferase, ALT=alanine aminotransferase, GGT=gamma-glutamyl transferase, TP=total protein

However, mean serum AChE activity and levels of albumin and total protein were significantly lower while mean serum activities of AST and ALT were significantly higher in PA compared with farmers (P = 0.000, 0.003, 0.017, 0.007, 0.001 respectively). Farmers and PA had similar levels of TBIL, CBIL, urea, creatinine and mean serum activities of ALP and GGT. In the PA group, there was no observed significant correlation between AChE and all the indices of renal and liver function (Table 2). However, only TBIL showed significant negative correlation with AChE in the farmers (Table 3).

DISCUSSION

Despite the vital role of Op in controlling agricultural, industrial, home and public health pests worldwide, its exposure continues to be a global public health issue (Rabideau, 2001; Weiss et al., 2004; Bjorling-Poulsen et al., 2008; Calvert et al., 2008). According to the World Health Organization, 3 million cases of pesticide poisoning occur every year resulting in more than 250,000 deaths (Yang and Deng, 2007).

The observed significant decrease in activity of AChE in PA and farmers compared with controls as well as in PA compared with farmers shows that depressed activity of AChE is a common feature of both PA and farmers but it is more severe in PA than farmers. Our result supports earlier findings of Aldridge (1971), Vidyasagar et al. (2004) and Reddy and Jagdish (2012). Adverse effect of Op has been linked with cholinesterase inhibition (Gbaruko et al., 2009) because it binds with cholinesterase enzyme and inhibits the activity of the enzyme by irreversible phosphorylation (Abou-Donia, 2003).

Due to the wide range of disorders that have been reported following Op exposure, some researchers believe that inhibition of AChE activity alone might not account for these disorders (Peeples et al., 2005). Therefore, hepatocellular and renal dysfunction may be other possible mechanisms for adverse health effects of Op toxicity.

Liver is a multifunctional organ involved in excretory, synthetic and metabolic functions which are essential to life (Burtis et al, 2006). Hepatocytes have an enormous regenerative capacity as well as a marked capacity to respond to increased metabolic demands but chronic exposure to pesticides may lead to accumulation of toxins in the liver and cause pathological alterations (Braun beck, 1994). Cell injury of certain organs like liver leads to increased release of tissue specific enzymes into the bloodstream, the degree of elevation varies with the type and extent of injury (Burtis and Ashwood, 1996). In this study, serum activities of AST and ALT were significantly higher in PA and farmers compared with the control subjects, and also in PA compared with farmers. The significant increase in the activities of transaminases (AST and ALT) in both PA and farmers implies hepatic damage. Altuntas et al. (2002) reported an increase in the activities of aminotrasferases in workers engaged in an agricultural programme. Increased activities of ALT and AST have been reported to be caused by leakage from injured hepatic cells; this necessitated their use as markers for liver damage (Reddy et al, 2010, Roxana et al, 2010, Reddy and Baghel, 2012). Gamma glutammyl transferase (GGT) is a clinically important liver enzyme in the differential diagnosis of liver injury. Its elevation has been reported to indicate hepatotoxicity in subjects exposed to environmental toxicants (Seth et al, 2001). This might explain the observed higher GGT activity in PA and farmers when compared with the control subjects. The liver is also the primary site of plasma protein synthesis including albumin. The pattern and direction of plasma protein alteration depends on type, severity and duration of liver injury (Burtis and Ashwood, 1996). In this study, TP and albumin were significantly lower in PA and farmers compared with the control subjects and in PA compared with farmers. This observation may indicate reduced synthetic function of the liver as a result of overwhelming metabolism of absorbed Op causing reduced synthesis of albumin, a marker for evaluation of synthetic capacity of the liver.

Urea is synthesized in the liver and the rate of hepatic urea synthesis depends on exogenous intake of nitrogen as well as on endogenous protein catabolism. The significant decrease in urea level observed in farmers compared with the control subjects may support our suggested Op-induced reduction in the synthetic capacity of the liver. Our general observation on indices of liver function, together with the inverse correlation of TBIL with AChE, suggests that farm workers exposed to Op are at risk of liver dysfunction.

Kidneys are a paired organ system with functions characterized as excretory, regulatory and endocrine. The excretory function serves to rid the body of non-protein nitrogenous compounds such as urea and creatinine (Burtis and Ashwood, 1996). The biosynthesis of urea is carried out exclusively by hepatic enzymes of the urea cycle but more than 90% is excreted through the kidneys. Creatinine, an indicator of kidney damage, was significantly higher in PA only compared with the control subjects. This observation might suggest renal injury in the PA. However, it must be noted that creatinine only is insufficient to define Op-induced renal toxicity. A battery of biochemical parameters would provide a better evaluation of the renal toxicity.

It can be concluded from this study that liver and renal dysfunction are associated with organophosphate pesticides exposure but pesticides applicators are at a higher risk of liver dysfunction than the farmers. Farm workers are therefore encouraged to use personal protective equipment (PPE) to reduce exposure to Op and may require periodic assessment of their liver and renal function.

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