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BLOOD ACETYL CHOLINESTERASE INHIBITION AMONG WORKERS EXPOSED TO FENTHION DURING AVIAN PEST CONTROLS IN THE SAHEL REGION OF BURKINA FASO, WEST AFRICA

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ABSTRACT

Fenthion is the main avicide used to control the red-billed quelea by spraying their roots. However, fenthion is highly toxic to non-targeted organisms.The main study objective was to evaluate the activity of acetyl cholinesterase (AChE) and hematological parameters (hemoglobin level: Hb) among the DPVC workers who used fenthion as an organophosphorus (OP) pesticides to control invasion of red-billed quelea in the Sahelian region of Burkina Faso. The acetylcholinesterase (AChE) and hemoglobin were evaluated as biomarkers exposure to OP by using kinetic method of Ellman. Then, the results of exposed group were compared with the unexposed one. Data showed significant difference in AChE activities between the two groups *(P*<0.001).Similarly, hematological parameter including Hb levels tested revealed significant statistical difference in the means of the two group (*P*=0.001). Nineteen applicators had high inhibition for cholinesterase activity in whole blood compared to the control group. The study raised a serious need of regular training of workers in how to efficiently use the equipments provided and also in what to do in case of accident.

KEYWORDS: red-billed quelea, AChE, organophosphorus pesticides, Burkina.

INTRODUCTION

Despite its importance, the agricultural sector in Burkina Faso has not experienced significant development since the independence days. Food security is not regularly ensured from one year to the next. The incidence of poverty remains high in rural areas where agriculture is most practiced. Such shortcomings are partially attributed to several biotic and abiotic stresses of various kinds.[1] In the Sahel region and part of the Mouhoun one, the biotic stress that qualitatively and quantitatively depressed crop yield is migrant pests which follow rainfall system. Especially, the red-billed quelea, which is the most important avian pest of small grain crop in Africa, causing significant economic loss through devastations in agricultural crops.[2] Thus, such danger is an abundant granivorous land-bird living in at least 20 countries of West, East, and Southern Africa. They usually occur in huge flocks that are capable of devastating cultivated small-grain cereals such as wheat, rice, sorghum and millet. They can cause damage up to the equivalent of US$ 88.6 million per year in semi-arid zones.[3] To control this avian pest, the Department of Plant Protection and Packaging (DPVC in French acronym) of the agriculture ministry of Burkina Faso routinely use fenthion 640 ULV (ultra low volume) by ground spraying the breeding colonies and roosts after dark when the birds have settled down for night.[3] However, fenthion as others organophosphorus (OP), has highly side effects on non-target organisms including human.[2–4] In addition, it is known to have negative effects on aquatic invertebrates, which predicates against its use near water bodies.[5] Intensive pesticide use has been associated with a variety of adverse health outcomes. Thus, OP insecticides are estimated to cause more than 100,000 deaths and 2 million hospital admissions every year, nearly all in developing countries.[6–9] Fenthion as other OP is a potent neurotoxic molecule because it inhibits neuronal acetylcholinesterase (AChE).[10–12] This enzyme hydrolyses the neurotransmitter acetylcholine and thus is essential for the proper functioning of the nervous system. Inhibition of the AChE enzyme causes an accumulation of acetylcholine in cholinergic synapses, inducing a continuous and excessive stimulation of acetylcholine receptors and thus leading to tremendous malfunctions of the body.[10] This state of permanent transmission of the influx nervous usually in human body can cause acute symptoms including nausea, breathing difficulties and even death. Consequently, measurement of the activity of the red blood cell AChE

is widely used for diagnosis of poisoning and adverse effects caused by OP.[13–19]

Due to of limited data in Burkina Faso related to human monitoring of pesticide exposure, the objective of this study was to evaluate the activity of AChE and hematological parameters (hemoglobin level: Hb) among workers who used Fenthion as an OP insecticide to control invasion of red-billed quelea in the Sahel region of Burkina Faso.

MATERIAL AND METHODS

Study design

Across sectional study was carried out in the Sahel region, located in the extreme north of Burkina Faso, between September and December 2016, period of attacks on small-grain crops by avian pests. During this period, the government has mobilized workers from DPVC to control the attacks by using fenthion 640g/l ULV as the formulation for the control as OP. Thus, in the present study, the toxic effect of occupational exposure to OP was analyzed using AChE activity in erythrocytes. It involved 88 workers in the age group of 22–58 years divided into two groups (confer table1).

-The exposed group: consisted of applicators occupationally exposed to complex mixtures of the pesticide (n=40). Their main roles were to prepare the pesticide mixtures and refill the tanks and to spray the breeding colonies and roosts of birds at night.

- The non-exposed group consisting of the supervisors (n=48) who were not systematically exposed to fenthion.

Before the determination of cholinesterase, general informations regarding the age, medical history, frequency and duration of exposure to fenthion were recorded. Those with a history of chronic disease, or taking antimalarial drug were excluded. Furthermore, the purpose of the research was explained to each participant and its verbal informed consent was obtained prior to blood sample collection.

Cholinesterase assay procedure

The activities of erythrocyte acetylcholinesterase (AChE) were performed using the photometricanalyzer Test-mate ChE® (EQM Research Inc., Ohio, USA). The Test-mate ChE® cholinesterase test system is based on kinetic method of Ellman *et al*.[21]. Briefly, the Acetylthiocholine (AcTC) or butyrylthiocholine (BuTC) is hydrolyzed by AChE or PChE, respectively, producing carboxylic acid and thiocholine which reacts with the Ellman reagent (DTNB, dithionitrobenzoic acid) to form a yellow color which is measured spectrophotometrically at 450nm. The rate of color formation is proportional to the amount of either AChE or PChE. The Model 460 AChE Assay Kit was used and for each blood test, 10µL were required which were obtained from a finger stick sample. The manipulation of the instrument was performed by a team of trained technician. The tests were performed under field conditions and results were instantly provided to the workers. Each morning, the performance of the instrument was made by using controls provided by the fabricant. In AChE mode, the analyzer gives six biological informations such as: amount of AChE (U/mL), percentage of AChE%, Hb level (g/dL), percentage of Hb %, ratio of level of AChE to Hb, (U/g) and the percentage derived from the ratio. For our study, only, AChE and Hb were recorded.

Ethics

Ethical approval for this study was obtained from the Central Region Directorate of Health, Ministry of Health Burkina Faso with approval number No.2017-01835/MS/RCEN/DRSC.

Statistical analysis

The benchmark for AChE was obtained for enzymatic activity of the enzyme in the non-exposed group. The inhibition values in percentage were calculated with the following formula: Inhibition values = ((AChEm – AChEp) / AChEm) x 100.

AChEm= the average value of the non-exposed group, AChEp = individual value of AChE in the exposed group. The biochemical and hematological parameters were presented in mean ± standard deviation (SD).

Statistical analysis was performed using R-Studio 8.10. The Ryan-Joiner test of normal distribution was used and the unpaired *t*-test tested for differences in the AChE and Hb between exposed group and non-exposed group. The statistical significance in the differences was judged by using $P< 0.05$.

RESULTS

A total of eighty eight (88) individuals were tested in this study. The group exposed to Fenthion was comprised forty(40) individuals while the non-exposed group included forty eight (48) control subjects (table 1). The average ages were 39 ± 11.7 years old for the exposed group and 41.5 ± 10.2 years old for the non-exposed group. More than fifty percent of exposed group were under 36 years old.

The activities of AChE and the Hb levels in exposed and non-exposed group were measured as shown in table 2. It is worth noting that AChE levels in humans range from 2.77 - 5.57 U/mL. The means of AChE for the exposed group and for unexposed group were 2.45 U/mL ± 0.53 and 3.46U/mL ± 0.45 respectively. There was significant difference in AChE activities between the two groups($P< 0.001$).Similarly, hematological parameter including Hb levels tested in the study group revealed the average of 11.8 (g/dL) ± 1.2 in the exposed group and 12.7 (g/dL) ± 1.0 in the non-exposed one. Results of the analysis indicate that there was significant statistical difference in the means of the two groups (P=0.001). The World Health Organization (WHO) estimating that anemia corresponds to an Hb level less than 12.9 g/dl in men (15 years of age and above), 80% (32/40) of applicators exposed to fenthion have been diagnosed as anemic.

The reference value of AChE was obtained for average value of unexposed group (n=48) over all but no stratified by gender. Thus, the value of 3.46 U/ml was the benchmarks for AChE. Thirty percent (30%) inhibition for total AChE was established in order to define inhibition of AChE among applicators, representing a cut-off value of 2.42 U/ml. We have considered a subject as presenting a hypo level of cholinesterase in the blood, if the requested AChE is reduced by at least 30% below the reference value. The test results of some applicators showed some depressed levels of AChE below the cut-off value. Nineteen applicators (47.5%) had high inhibition for cholinesterase activity in whole blood from exposed group compared to the non-exposed one. Moreover, four individuals (10%) in the first group showed a very high inhibition (>50%) and 01 person had severe depression (80%) of his cholinesterase level.

Tables

Table 1: Sociodemographic characteristics of the study population

Characteristics	Exposed group (n=40)		Unexposed group (n=48)	
	n	%	n	%
gender				
Male	38	95	44	91.7
Female	2	5	4	8.3
Age (year)				
< 36	21	52.5	22	45.8
[36-50]	9	22.5	12	25
>50	10	25	14	29.2

Table 2: Activity of AchE and Hb levels in the two groups.

Parameters (mean ± SD)			
Parameters	**Exposed Group (n=40)**	**Unexposed Group (n=48)**	**P-value**
AChE Range	2.39 ± 0.53 0.59-3.57	3.46 ± 0.45 2.42-4.73	<0.0001
Hb Range	11.8 ±1.2 9.0-14.0	12.6±1.0 10.5-14.50	0.0001

DISCUSSION

WHO recommends the determination of the activity of AChE in the total blood as a reference method for monitoring the occupational exposure to OP.[22] In the absence of any clinical signs, this enzyme is a good biological marker used to confirm human degree of exposure to pesticide. Thus, monitoring the AChE activity is important stool in order to prevent or to treat pesticide poisoning. However; results of AChE have shown broad variability from benchmarks among subjects. It is therefore necessary to determine individual baseline measurements prior to an exposure period and then to compare the new values during or after exposure with the baseline.[23] In our study, we were not able to determine these baselines due to logistic problems. Nevertheless, we overcame this short coming by making the reference value of AChE with the average value of non-exposed group, representing the value of 3.46 U/ml. AChE levels in humans range from 2.77 - 5.57 U/ml. It should be noted that AChE levels are influenced by factors such as ethnic origin and the altitude above sea level of populations, and inter-individually by demographic and genetic factors.[24] On the other hand, certain clinical, sociodemographic, biochemical and hematology parameters should have been collected in order to detect persons with some diseases (liver disease for example) which might interfere the AChE activity.[24] Despite all these limitations it is possible to draw conclusions about the overall health risks of the fenthion exposures.

The present study found a significant difference in AChE activities between the two groups (P< 0.001). These results are in agreement with finding of various studies from several part of the world.[24–29] Similarly, Hb levels tested in the study group revealed that there was significant statistical difference in the means of the two groups (P=0.001). This result is consistent with lot of results reported in the literature.[24,29–33] AChE is essential enzyme for the normal functioning of the central and peripheral nervous system. Indeed, its activity is useful to terminate synaptic transmission and by the way preventing continuous nerve firings at nerve ending. Thus, OP pesticides bind irreversibility the esteratic site of enzyme by phosphorylation and inactivate it. As a result acetylcholine level accumulate in the muscles resulting in the development of symptoms that have their origin at different parts of the nervous system[10], On the other hand, this study revealed that nineteen (47.5%) cases of hypocholinesterasemia among the exposed group. These persons exhibited higher inhibition rate or equal to 30% compared to the reference value, but without generating any in these subjects muscarinic and nicotinic effects. Our results are consistent with experimental and epidemiological studies reporting an inhibition of AChE in group exposed to

pesticides.[15,34,35] Particularly, Mamadou *et al*.[36] evaluated 103 OP applicators during locust control in Niger and found that 16.50% had inhibited AChE. In addition, four applicators (10%) had very high inhibition (>50%). These workers were removed from avian control campaign as recommended. Among them, 01 worker had severe depression (80%) of his cholinesterase level. Ours investigation allowed us to find that this worker have had dermal exposure of huge quantity of fenthion during spraying operation by accident. According to MacFarlane *et al*.[37], health effects resulting from pesticide exposure vary according to the individual pesticide involved and may be the result of exposure via the dermal, oral, or inhalational routes; however, dermal exposure is the most relevant route of exposure for pesticide applicators. Although these 4 pesticide applicators did not show clinical symptoms, they were treated in the primary setting by administration of atropine.[38]

Maroni *et al*.[40] have found relationships between AChE inhibition and health negative effects. Thus, in agreement with their findings, a dose-response pattern of relatively mild symptoms such as weakness, headache, dizziness, nausea, and salivation with a convalescence of 1–3 days are elicited when the inhibition of AChE is between 50% and 60%. 90% decrease is considered severe poisoning and can be lethal from respiratory or cardiac failure.

The results of this study raised serious concerns about the training of applicators the DPVC. Indeed, the potential health hazards may be arisen as a result from inadequate education, training and safety systems. Thus, regular training and supervision of o pest control personnel on correct use of equipment in order to minimize excessive contamination of environment and risk to personnel. According to our observations, in the fight against avian pests, the agents (mostly applicators) are not enough protected or poorly protected. In addition, we have noticed during this study that even if protective equipments are available, they were not suitable for the climatic conditions which militate against their wearing. Evidently, appropriate equipment and necessary precaution during all stages (mixing, loading, transporting and spraying) could help to minimize worker exposure to fenthion. Furthermore, as this OP has high toxicity to wildlife and human, it is necessary for DPVC to develop or test alternative avicide that is more specific to quelea.

CONCLUSION

The main determinants of pesticide exposure levels that could be demonstrated are the type of work, the quality of the protective equipment, the duration of the exposure, the educational level of the worker and the number of exposures. Despite all the limitations in this study it is possible to draw conclusions about the overall health risks of the fenthion exposures. Results of the analysis during this study indicated that there were health risks in the exposed groups.

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Conflicts of Interest: The authors declare no conflict of interests.

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