Alterations in Blood Cholinesterase and Liver Function During Occupational Exposure to Pesticide

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ABSTRACT

A bio-monitoring programme for workers with occupational pesticide exposure was undertaken. Blood cholinesterase levels were determined in all the workers from the Public Health Directorate, Bahrain, irrespective of the duration of exposure, age and type of pesticide used by each of these workers. The longest exposure is approximately seven years and reaches its height during the vector breeding season, i.e. twice a year each time for the duration of one month. The significance of blood cholinesterase estimation is high in chronic pesticide exposure, especially during and after the active spraying of organophosphate and usage of carbamate pesticide. It constitutes a good bio-monitoring system, valid in terms of both health and safety, in occupational exposure.

The control of vectors by pesticide remains a major component of disease control programmes. Pesticide use for public health has gained importance and priority in most developing countries. However, their usage remains proportionately greater in the developed countries. Problems of resistance to pesticides and questions of safety and environmental pollution directly affect sales of pesticides to developing countries. These have become matters of concern for both industry and health bodies. Most recent programmes have encouraged the use of newer and more varied pesticides in agrochemical industries for trials and development as WHO priority needs.

Public concern over safety, the undesirable effect of vector control and environmental pollution are constraints which are chosen depending on a country's social, financial and scientific development. In Bahrain, since 1976, job opportunities in pesticide promotion programmes have resulted in greater occupational exposure to workers actually handling the finished product. Good industrial hygiene and effective protective measures have been laid down for all pesticide surveillance programmes. Proof of their effectiveness depends upon suitable biological monitoring systems.

In this study, the importance of assessing the overall health status of all pesticide handlers and determining their blood cholinesterase levels has been attempted. The exposure has been to a random number of pesticides used over the past seven years. They include a mixture of pesticides belonging to different chemical catagories.

METHOD

A list of the usage of all pesticides and insecticides was obtained from the Environmental Health Section of the Public Health Directorate. This list of chemicals for vector control is tabulated in Table 1.

A list of all the people actually employed for the purpose of spraying and handling of these chemicals was also obtained. A general clinical check up was carried out. In the field survey of exposure to pesticide, the protocol was based on the guidelines as laid down by the WHO VBC/82.1 [7].

For biological monitoring, basal biochemical and haematological parameters were assessed by referring them to the Salmaniya Medical Centre Pathology Laboratory. Cholinesterase estimations in all the employees were carried out in the Public Health Laboratory. These were first done when the workers were not specifically using malathion and carbaryl and later when they were actively using these compounds, during the spring season. The first set of readings gave basal resting values of cholinesterase. The second set of values were obtained on the day of the spraying to obtain peak values of cholinesterase in blood immediately after spraying.

A third assessment of cholinesterase was completed in some workers, to observe the trend in recovery, a month after the spraying session was over.

The cholinesterase was estimated by the Tintometric cholinesterase kits produced by Tintometers Sales Ltd., Salisbury, U.K.. It is based on the principle that

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TABLE 1 — INSECTICIDES USED BY MALARIA & INSECT CONTROL SECTION

COMMON NAME	CHEMICAL NAME	CHEMICAL FORMULATION	ANTIDOTE	PREPARATION & USAGE	GENERAL NOTES
Propoxur 50% W.P. 1% Fly Bait Moderately hazardous Baygon 50 w.p.	2 — Isoptopoxyphenyl-N-Methylcarbamate	$C_{11}H_{15}NO_3$	Atropine	Wattable powder + 100g per gallon of water used as spray by knapsack sprayer	Carried by labourers in small cans in order to be mixed with water directly in the machine on sites of work where water is available for mixing and washing.
Denkavepon, Dechloroves, D.D.V.P. NUVAN Highly hazardous VBC/78 1Rev 3 (Not used in the last 3 years)	O,D,-dimethyl — 0 — (2,2 dichlorovinyl) Phosphate	$C_4H_7O_4Cl_2P$ Organophosphate	Atropine	S.C. + Kerosine — fogging 150 oz. DDVP 100sc + 1gal. Kerosine 1½oz DDVP 98EC + 1gal.water	Carried by Anti-fly labourers as liquid concentrate in glass — closed bottles to be mixed with water directly in the spraying machines or to be mixed with kerosine at the main store and then given to the labourers in drums to be used in fogging machines.
Reslin 25S ULV Concentrate. Slightly hazardous	Permethrin + S.Bioallethrin + Piperonyl Butoxide	Carbamate Synthetic Pyrethroid	Not known	1 part Reslin + 9 parts Diesel oil	* Used by special ULV generators after being mixed at the main store * Sprayed as very fine droplets of optimum size. * Used specially for markets, hospitals and other places of importance.
Pybothrine 8/64 or Neopybuthrine S 200-Q Slightly hazardous.	0.8% S.Bioallethrin 2.8% Permethrin 4.0% Piperonyl Butoxide	Carbamate Synthetic Pyrethroid	Not known	1 part Pybothrine + 200 parts of Kerosine or Diesel oil	* Mixed at the main store with Diesel oil or with Kerosine. * Carried by the labourers in 10 gallons drums to be used as larvacidal oil or fogging flit.
Malathion 50% w.p. Slightly hazardous	O.O-dimethyl hydrogen phosphorodithioate + diethyl maleate hydroquinone	$C_{10}H_{19}O_6PS_2$ Organophosphorus (OP)	Atropine	200g. Malathion 50% + 1gal water	* Used as residual insecticides * Sprayed by the knapsack sprayers on walls and other surfaces where mosquitoes rest. * Mixing of the insecticide with water is done on the site of work in 45 gallon drums. * The powder is carried in small steel drums with covers.
Acetellic 2% dust Moderately hazardous	Primiphos-methyl	Organophosphorus	Atropine	Ready for use	In powder form used specially for crawling insects.
Dustex 1-2% dust Carbaryl 5% w/w Moderately hazardous	1-naphtyl N-methyl-carbamate	Carbamate	Atropine Sulfate	Ready for use	Applied either directly from the packets or by dusting pump. Distributed to the public in paper packet with the instructions painted on them
Triton X-45 emulsifier Spreading Agent	Octylphenoxypolyethoxyethanol	Organic	—	10% Triton X-45 + 90% Diesel Oil	Mixed with larvacidal oil at the main stores.

Acetylcholineiodide is used as a substrate and hydrolysed to thiocholine iodide and acetic acid. Both erythrocyte and plasma cholinesterase hydrolyse acetylcholine, liberating acetic acid and thereby changing the pH. This is indicated by bromothymol blue indicator and compared in a Lovibond Comparator Disc. These estimations were obtained from a finger-tip blood sample.

RESULTS

The list of insecticides as used by those working with the Environmental Health Section of the Public Health Directorate, shows that they are chosen in accordance with the guidelines to the use of the WHO recommended classification of the pesticides by hazard and usage [6].

Table II A shows the distribution of cholinesterase actively present, as a percentage of the proportionate depression from the normal, for each individual as a function of age and duration of exposure. These values are an average of duplicate values and represent basal levels for each individual. 12.5% depression in individual workers represents normal fluctuation and inherent variations in the method.

Slight to moderate depression of 25% and moderate to pronounced depression of 37.5% are also recorded.

TABLE II - A

CHOLINESTERASE ACTIVITY	AGE GROUP	DURATION OF EXPOSURE TO PESTICIDE					VR
		1 to 2 yrs	3 to 4 yrs	5 to 6 yrs	7 to 8 yrs	8 yrs >	
100%	20 to 29	5	2	23	10	3	6.4
	30 to 39	4	3	13	4	4	
	40 to 49	1	1	9	5	8	
	50 to 59	—	—	5	—	2	
100% — 87.5%	20 to 29	1	—	9	3	1	3.3
	30 to 39	—	1	9	4	4	
	40 to 49	—	—	2	1	4	
	50 to 59	—	—	—	—	4	
87.5%	20 to 29	2	2	6	4	2	4.6
	30 to 39	1	1	5	—	8	
	40 to 49	1	1	3	2	9	
	50 to 59	—	—	—	1	6	
87.5% — 75%	20 to 29	2	1	8	6	1	1.7
	30 to 39	2	—	5	—	1	
	40 to 49	—	—	2	—	2	
	50 to 59	—	—	—	—	4	

Table II B shows the cholinesterase activity by age group in samples obtained immediately upon completion of spraying of malathion. These were obtained in the work place and the inherent variation in the method is expected to be high because of the vagaries of field work. It also shows the cholinesterase activity of some of these workers four weeks after the last day of spraying and shows the trend to recovery towards normal basal levels.

During these biochemical studies the workers have otherwise remained asymptomatic and carried out normal routine duties.

TABLE II - B

CHOLINESTERASE ACTIVITY	AGE GROUP	BASAL	IMM AFTER	4WKS LATER	VR
	20 to 39	111	4	8	3.6
100%	40 to 59	41	5	3	7.7
	20 to 39	56	35	5	
100% — 87.5%	40 to 59	27	15	1	
	20 to 39	0	28	3	
87.5% — 75%	40 to 59	0	7	2	
	20 to 39	0	9	0	3.10
62.5%	40 to 59	0	3	1	1.31
	20 to 39	0	2	0	
50%	40 to 59	0	1	0	

Table III shows the normal distribution of the Serum Glutamate Oxalocetate Transaminase (SGOT) and Serum Glutamate-Pyruvate Transaminase (SGPT). It shows a normal distribution of these enzymes and liver function.

Table IV is a compilation of SGPT versus cholinesterase activity.

The analysis of the presented data was based on bio-statistical hypothesis testing. The "null' hypothesis "Ho", was tested for all the variables, i.e. age, duration of exposure, enzyme activity and liver function. This was carried out after distributing the data in the form of the randomised complete block design. A computer programme was developed for the randomised complete block design to obtain the variance ratios. The computed variance ratios for these blocks were found to be greater than the critical value of F (.975) wherein $P < .005$ and are therefore, highly significant.

TABLE III

SGOT	SGPT				V.R.
	1-24	25-49	50-74	> 75	
25 to 41	157	32	2	—	
42 to 60	7	16	8	—	
61 to 80	—	—	1	2	.97
80	—	—	—	3	

TABLE IV

CHOLINE-STERASE	SGPT				V.R.
	1-24	25-49	50-74	75	
100%	72	22	5	1	16.2
100% - 87.5%	32	6	1	—	
87.5%	40	13	5	2	
87.5% - 75%	25	5	2	1	

DISCUSSION

The kind of pesticides to which the workers of this study were exposed, are a heterogenous group of chemicals used for over seven years and more specifically to the organophosphates and the carbamates. The most important bio-indicator of organophosphate and carbamate exposure is its influence on anticholinesterase kinetics. Acute organophosphate insecticide poisoning is well known by its clinical findings and concomittant bio-chemical changes that can have manifestations of severe hyperglycemia, severe metabolic acidemia and moderate hypokalemia [3].

Subthreshold exposure, as occurs in occupational situations, warrants regular monitoring of these people, even when totally asymptomatic. The design of a suitable monitoring system required a good knowledge of the biological actions of the compounds in use [4] and the metabolic pathways as followed by them within the biological system [5].

A decreased serum cholinesterase activity may also occur if hepatobiliary dysfunction interferes with the synthesis of this enzyme. It is of established clinical value in suxamethonium sensitivity and liver disease.

Cholinesterase estimation in field situations is an easy and convenient parameter. The reliability of this has been discussed time and again since its significance was initially brought to light [2]. Its regular estimation as part of the periodic medical examination has been carried out in Cuba [1], The State of California, U.S.A. and elsewhere.

CONCLUSION

As a bio-monitoring system for pesticide exposure in Bahrain, in its target population of workers at the Public Health Directorate, it has been a study of some academic and practical significance. The regular monitoring of blood cholinesterase in the actual sprayers (who devote two months a year to the use of organophosphates at an average of three hours per working day) constitutes a good screening programme.

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