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Carbamates Toxicity in Farmers and its Assessment Through Biochemical Parameters

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Abstract

Prevalent environmental toxicity of various chemical groups of pesticides and their effects leading towards increasing morbidity and mortality in the farmers is of great concerned. In this situation the biochemical biomarkers are regarded as meaningful tools for monitoring toxic end points. This work was aimed to assess the toxic impacts of carbamates through some biochemical parameters and useful validity of these biomarkers was also observed. Present results reveal inhibition of cholinesterase activity by 46%, whereas bilirubin, urea and creatinine levels in serum were increased and sugar values was decreased at highly significant level ($p<0.001$). Urine urobilinogen concentration found raised significantly at high level ($p<0.001$) while protein, urea, creatinine and sugar values in urine of the farmers seen non-significant. This study concluded that the selected biochemical parameters can be used as biomarkers to assess the significant toxic effects in the exposed populations.

Keywords: Carbamates, Biochemical biomarkers, Farmers in Pakistan

Introduction

Farmers in local areas of Sindh province of Pakistan occupationally active as spray workers are facing pesticide induced health problems in consequence of toxic exposures. They are not environmentally aware about pesticide hazards, therefore, their perceptions of relative toxicity differ from the probable risk. Carbamates group of pesticides is well absorbed from all routes of exposure. Its poisoning may occur from inhalation, oral, dermal, or ocular exposure; however, these compounds are more toxic by ingestion than by dermal contact [1]. Massive use of carbamates can result the health impairment due to direct or indirect exposures to the farmers. Widely used carbamates like carbaryl, methomyl, propoxur and aldicarb, are suspected carcinogens and cause lung, kidney and liver damage, these are neurotoxic and affect the immune system as well [2 – 4].

According to laboratory findings; changes in cholinesterase activity, along with the typical signs and symptoms, provide sufficient information for the diagnosis and management of carbamates poisoning cases [5]. The significant changes due to carbamates in some of the biochemical parameters have been reported in animals [6] and in the suicide attempting human subjects [7]. But less attention was paid towards the carbamates toxic effects and its assessment methods in the massively exposed farmers. Present work was aimed to observe the toxic effects of this group of pesticides and validity of some biochemical parameters for exposed farmers in the local environment.

Materials and Methods

Sample Collection

Total 108 of blood samples 3ml in quantity were collected by vein-puncture method from the subject farmers (n=58) who were exclusively exposed to carbamates group of pesticides and age

matched controls (n=50) who never exposed to any chemical pesticides were selected from various distant areas of Sindh province of Pakistan. All the samples were transferred into sterilized screw caped glass tubes and allowed to clot, then centrifuged at 3000 G to obtain the serum for analysis. Both the groups were further asked and advised to wash their groin properly and void mid stream urine. After voiding urine in 50 ml sized screw caped glass bottles, the samples under sterile conditions were transferred to laboratory for required analysis.

Spectrophotometric Analysis

Spectronic 20 (Bouch and Lumb) was used to determine the biochemical values of serum cholinesterase activity, total protein, urea, creatinine and sugar while urine samples were analyzed for protein, urea, creatinine and sugar. All the chemical reagents in the form of prepared kits used for biochemical analysis were purchased from Merck, Germany.

Statistical Analysis

Statistical analysis was carried out by computer program version 8.0 of SPSS. Differences between subject and control groups were assessed by student t-test and were accepted as significantly different at $p<0.01$.

Results and Discussion

The development of biomarker stems from efforts to identify the physiological and biochemical changes in the exposed population. The ideal and valid biomarker is one which indicates a biological response and is not just a measurement of chemical / metabolite residues. Results of this work show inhibition of cholinesterase activity by 46% in the subject farmers as compared to controls. Table 1 (a) shows Mean ± S.D for both the groups and probability ($p<0.001$), which is highly significant. According to recommendations of WHO as well other workers, the inhibition of cholinesterase activity by 30% of pre-exposure/control level should be regarded as biological exposure limit [8]. As carbamates group of pesticides inhibits cholinesterase enzymes so mostly observed in occupational poisoning cases among plantation workers and farmers [9]. Thus, in 1990, Jeyaratnam [10] estimated that about 3% of agricultural workers in developing countries suffer an episode of symptomatic poisoning every year.

Some authors [11-14], reported the inhibition of acetylcholinesterase as a key step in the mechanism of toxicity of certain organophosphate and carbamate pesticides therefore, measures of this parameter represent a critical biochemical biomarker of potential adverse effects. In view of above citations and present work, this biomarker was indicated as consistent to early work and valid to see the toxic impact of carbamates in the farmers.

The subject farmers were seen with raised values of bilirubin in serum and urobilinogen levels in their urine samples at highly significant level ($p<0.001$) as shown in Table 1 (b) and Table 2 (a). Serum bilirubin values are raised only if liver is considerably damaged due to; drugs and poisons, hepatic failure, viral hepatitis and in case of bile duct obstruction with cholestasis [15]. As present work shows such changes in this biochemical parameter that indicate the hepatotoxic consequences of carbamates group of pesticides in the local farmers.

Present work indicates non-significant effects on serum total proteins (Table 1(c)) and no significant changes were detected in urine protein concentration (Table 2 (b)). Though, hundreds of proteins in blood circulation experiences through the variations in different physiological and pathological conditions [16-17]. Certain nephrotoxic chemicals may be pesticides, disrupt the key functions of kidney and allow proteins to appear in urine thus the proteinurea causes hypoproteinemia. Other possibility is impaired hepatocellular function in which decrease in protein synthesis may occur. These results show no considerable injury either to the liver or kidneys by this biomarker in the farmers exposed to carbamates, whereas its validity need further investigation with reference to organophosphates.

Table 1(d) reveals the serum urea concentration level in serum was decreased significantly ($p<0.001$) at high level but in urine

the changes in values can be seen non-significant (Table 2 (c). Urea is the end product of protein metabolism, its concentration falls in urine and rises rapidly in serum due to acute renal impairment. In case of uremia concerned with intrinsic renal disease the glomerular filtration rate diminishes and leads to urea retention and may rise its' level. Decreases in serum urea are seen in severe liver disease with destruction of cells leading to impairment of the urea cycle [18]. Hence present work unveiled the hepatotoxic effects of carbamates in the subject group of the farmers and usefulness of the parameter.

Results of this study show no significant effects of the carbamates on creatinine concentration in serum and urine of the farmers (Tables 1(e) & Table 2(d). Although creatinine is considered more reliable guide in renal functions; as it is produced from muscle at a constant rate and almost completely filtered at the glomerulus and not reabsorbed in the tubules. Reduction in creatinine values is caused by conditions of acute glomerulonephritis, shock, hypovolumea and nephrotoxic chemicals. Soomro *et al.* reported increase in serum creatinine values, which indicated its effects on kidneys only [19], thence information persists for suitability of this biomarker as well.

The advanced qualitative and quantitative glucose determination methods based on 'Glucose oxidase' are preferred and applied to serum and urine because it has detectable sensitivity to minimum amounts of glucose range from 0.01– 0.1 percent. Results obtained by this method are given in Table 1 (f), which reveals the reduced level of serum sugar in the farmers who sprayed the carbamates, hence highly significant ($p<0.001$) whereas no significant change was found in urine of the farmers (Table 2 (e). Glucose is a main carbohydrate substrate, stored as glycogen in muscle and liver when reach there through circulation. It has been suggested that the body has cells, called glucoreceptors that monitor the level of glucose in the blood [20]. Hence the significant effects of the carbamates measured in this work can be assumed to affect the monitory system of glucoreceptors in the body. Therefore this parameter may also be considered as one of the valid biomarkers in assessing the carbamates toxicity in the exposed population including farmers.

Table 1 Effects of carbamates on serum biochemical parameters of farmers as compared to controls.

Serum Parameters	Farmers (n=58) Mean ± S.D	Control (n= 50) Mean ± S.D	p-value
(a) Cholinesterase μ/ml	1.53 ± 0.28	3.32 ± 0.66	<0.001
(b) Bilirubin mg/dl	2.17 ± 0.51	0.78 ± 0.18	<0.001
(c) Total protein mg/dl	10.02 ± 1.13	7.44 ± 1.33	N.S
(d) Urea mg/dl	14.93 ± 1.91	28.70 ± 5.48	<0.001
(e) Creatinine mg/dl	1.93 ± 1.46	0.97 ± 0.21	N.S
(f) Sugar mg/dl	48.79 ± 23.94	98.71 ± 6.10	<0.001

Table 2 Effects of carbamates on urine biochemical parameters of farmers as compared to recommended normal ranges and controls.

Urine Parameters	Farmers (n=58) Mean ± S.D	Control (n= 50) Mean ± S.D	p-value
(a) Urobilinogen (mg/24 hr)	3.93 ± 1.85	1.90 ± 0.42	<0.001
(b) Protein (mg/24hr)	76.25 ± 19.46	37.17 ± 17.75	N.S
(c) Urea (g/24 hr)	24.89 ± 2.31	28.27 ± 6.25	N.S
(d) Creatinine (g/24hr)	1.59 ± 0.80	0.78 ± 0.18	N.S
(e) Sugar (mg/dl)	16.29 ± 7.34	11.08 ± 4.46	N.S

Conclusion

Biochemical tests conducted on blood and urine samples of the farmers have shown the effects of carbamates. Significant differences in the values of selected parameters indicated their effective and valid role in chemical toxicity particularly in agriculture environment including

farmers population. With little expansion towards the symptomatic inclusive studies the non-significant changes may also be useful indicators to understand the organs/system affected level in the exposed farmers. Conclusively the assessment carried out by biochemical parameters for carbamates group of pesticides in this work may be considered as useful biomarkers.

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