Section: General Medicine

Original Research Article

SEVERITY AND PROGNOSIS OF ACUTE ORGANOPHOSPHORUS PESTICIDE POISONING INDICATED BY C-REACTIVE PROTEIN and ACUTE PHYSIOLOGY AND CHRONIC HEALTH EVALUATION (APACHE) II SCORE

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Abstract

Background: Organo-phosphorus compounds (OPC) are widely used insecticides, causing nearly 50% of emergency department admissions due to their toxicity and lack of medical facilities. Diagnosis and treatment are based on symptoms, laboratory tests, and plasma C-reactive protein (CRP) levels. This study aimed to investigate the plasma levels of C-reactive protein and assess the severity and prognosis of acute organophosphorus pesticide poisoning using C-reactive protein levels and the APACHE II score. **Material and Methods:** This prospective study was conducted on 100 organophosphorus pesticide-poisoned patients admitted to the Govt Rajaji Hospital Madurai from February 2019 to September 2019. Routine urine, complete blood count, blood sugar, urea, creatinine, Lft, proteins, electrolytes, ABG, choline esterase, and C-reactive protein were recorded. **Results:** The mean differences in serum choline esterase levels, CRP, and APACHE II scores between mild and moderate severity were statistically significant with a p-value of 0. There were significant differences in neck muscle weakness, ventilator requirement, and outcome ($p = 0.001$). The overall logistic regression model was statistically significant ($x2 = 69.3$, $p = 0.001$*), indicating that the predictor variables included in the model reliably differentiated between subjects in terms of prognosis. CRP levels at admission, 24 h, and 48 h, as well as serum choline esterase levels, were significantly associated with the severity of the condition assessed by the APACHE II score. **Conclusion:** Increased levels of C-reactive protein in patients with severe acute organophosphorus pesticide poisoning are significant for the prediction of severity and prognosis in patients with acute organophosphorus pesticide poisoning.

INTRODUCTION

Organo-phosphorus compounds (OPC) are widely used insecticides all over the world. According to statistics, nearly 50% of admissions for acute poisoning in the Emergency Department are due to organophosphorus compounds. Their accessibility and sociocultural factors play a considerable role in the selection of these compounds as the main suicidal agents. Poisoning with this substance is the most common cause of in-hospital mortality in developing countries such as India. The toxicity of these compounds and the lack of appropriate medical facilities have led to a high fatality rate.

The WHO Health Organization estimates that approximately 3 million people are exposed to pesticide poisoning every year, with approximately 2,00,000 lakh deaths per year in developing countries. India has the highest incidence of OPC poisoning worldwide; nearly 90% of poisoning cases are suicidal, with a fatality rate of >10%; 8-10% accidental, and 1% homicidal. Occupational exposure accounts for one-fifth of accidental poisoning cases, with fatalities of <1%. A history of exposure and signs of cholinergic overactivity can

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help diagnose this poisoning. Treatment includes physiological antagonism with atropine or glycopyrrolate and oxime, which helps to reactivate the enzymes. Complications, such as respiratory failure, CNS depression, and ventricular arrhythmias, should be anticipated and treated.

OPC poisoning is associated with cardiac complications, most of which occur in the first few hours of exposure. Hypoxaemia and electrolyte derangement also contribute to these complications. Organophosphates have been found to cause myocardial necrosis (myocardial toxicity). If poisoning is recognised early and effectively treated, complications can be prevented. Organophosphate compounds also influence neural dysfunction and brain damage by altering the normal internal milieu which leads to altered levels of consciousness in such poisoning. Acute organophosphorus pesticide poisoning (AOPP) is one of the most common acute medical conditions, with complex symptoms and a high mortality rate. Patients with Acute organophosphorus pesticide poisoning typically exhibit mortality-associated complications, such as secondary infections, myocardial injury, liver-kidney dysfunction, and multiple organ failure.

Currently, the severity of acute organophosphorus pesticide poisoning is usually evaluated based on patient symptoms, including dizziness, headaches, nausea, vomiting, salivation, sweating, blurred vision signs of fatigue, and routine blood and urine laboratory tests. Urine tests typically assess organophosphorus metabolic product content. In addition, the determination of cholinesterase levels in the plasma of patients with acute organophosphorus pesticide poisoning is widely used in the clinical diagnosis, treatment, and prognosis prediction of acute organophosphorus pesticide poisoning.

C-reactive protein (CRP) is a reactive substance in acute lesions, and elevated plasma CRP levels are a result of inflammation and trauma. In Acute organophosphorus pesticide poisoning, toxins may cause lesions in the tissues and organs of the body, leading to increased plasma CRP levels. Therefore, plasma CRP levels may reflect the severity of lesions caused by acute organophosphorus pesticide poisoning

Aim

This study aimed to investigate the plasma levels of C-reactive protein and assess the severity and prognosis of acute organophosphorus pesticide poisoning using C-reactive protein levels and the APACHE II score.

MATERIALS AND METHODS

This prospective study was conducted on 100 organophosphorus pesticide-poisoned patients admitted to the Govt Rajaji Hospital Madurai from February 2019 to September 2019. The study was approved by the institutional ethics committee before initiation, and informed consent was obtained from all patients.

Inclusion Criteria

All patients who ingested organophosphorus pesticides, history of exposure to organophosphorus pesticides, typical clinical manifestations and symptoms of organophosphorus pesticides, symptom improvement following treatment with the reactivating agent, and reduction in activity of cholinesterase were included.

Exclusion Criteria

Patients with infections, autoimmune diseases, inflammatory bowel diseases, and malignancies were excluded.

Routine urine, complete blood count, blood sugar, urea, creatinine, Lft, proteins, electrolytes, ABG, choline esterase, and C-reactive protein were recorded.

Statistical Analysis

The data were analysed using SPSS Version 17.0. Descriptive statistics were performed, and data were analysed to assess normality using the Shapiro-Wilk test. Based on the distribution of the data, a one-way analysis of variance (ANOVA) test was used for intergroup comparison of severity scores with other continuous variables. A post-hoc Tukey HSD test was performed to ascertain which pairs of severity score groups differed significantly from one another. Statistical significance was set at $p < 0.05$.

RESULTS

The mean age was the highest in the severe category, with a significant standard deviation, indicating a wide age range in this group. There was a substantial decrease in the mean value as the severity increased, indicating a potential correlation between severity and serum cholinesterase levels.

CRP at admission, 24 h later, and 48 h later: The mean CRP levels increased with severity and over time, suggesting a correlation between severity and CRP levels. The mean score increased significantly with severity, indicating a strong association between severity and the APACHE II scores. [Table 1]

The mean age difference between mild and moderate severity groups was statistically significant, with a p-value of 0. The mean age difference between the moderate and severe groups was not statistically significant ($p = 0.462$). The mean differences in serum choline esterase levels, CRP, and APACHE II scores between mild and moderate severity were statistically significant with a p-value of 0. [Table 2]

There was no significant difference in sex ($p = 0.107$). There were significant differences in neck muscle weakness, ventilator requirement, and outcome ($p = 0.001$). [Table 3]

The mean age of the expired patients was significantly higher than that of the live patients. The mean serum cholinesterase level of expired

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patients was significantly lower than that of live patients. The mean CRP levels of the expired patients were significantly higher than those of the live patients at all three-time points. The mean APACHE II scores of the expired patients were significantly higher than those of the surviving patients. [Table 4]

Univariate and bivariate logistic regression analyses comparing patients as predictors of prognosis. The overall logistic regression model was statistically significant (x2 = 69.3, p = 0.001*), indicating that the predictor variables included in the model reliably differentiated between subjects regarding prognosis. [Table 5]

There was a strong positive correlation (r=0.79) between CRP levels at admission and the APACHE II score. A strong positive correlation (r=0.914) was observed between CRP levels at 24 h and the APACHE II score. Similar to CRP at 24 h, there was a very strong positive correlation (r=0.924) between CRP levels at 48 h and the APACHE II score. There was a strong negative correlation (r=-0.742) between serum choline esterase levels and the APACHE II score. [Table 6 and Figures 1-4]

ROC, receiver operating characteristic; APACHE II, Acute Physiology and Chronic Health Evaluation II; CRP, C-reactive protein. Statistical significance was indicated when the area under the ROC curve was >0.5. [Table 7]

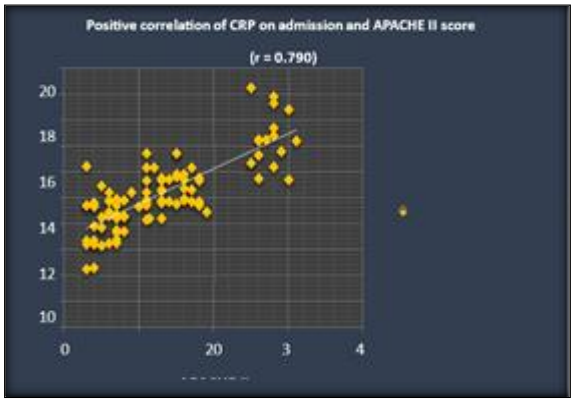

Figure 1: Correlation of CRP on admission and APACHE II score

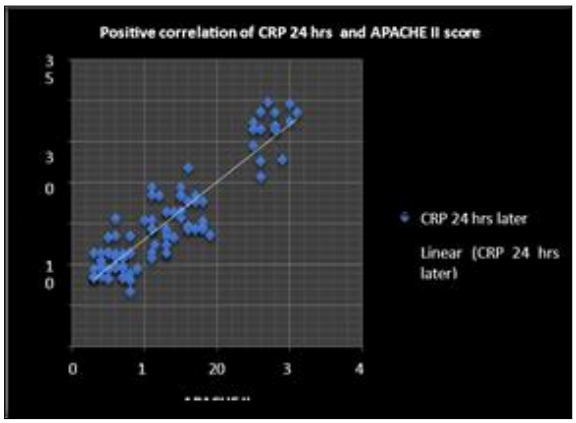

Figure 2: Correlation of CRP 24 hours and APACHE II score

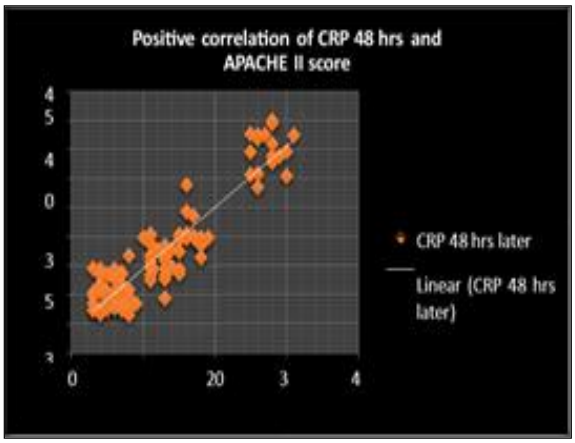

Figure 3: Correlation of CRP 48 hours and APACHE II score

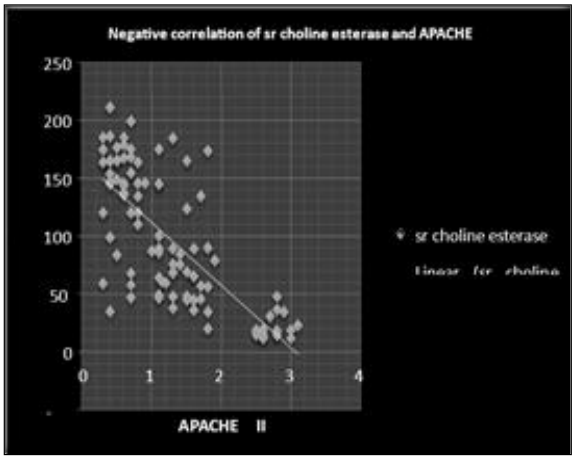

Figure 4: Correlation of serum choline esterase and APACHE II score

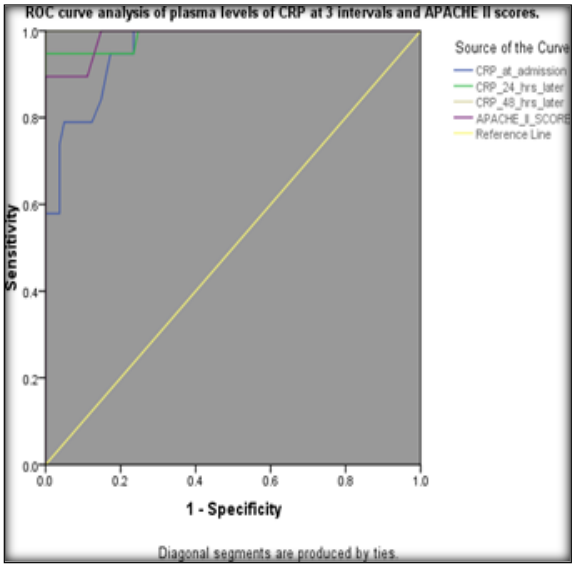

Figure 5: ROC curve analysis of plasma levels and CRP at 3 intervals and APACHE II scores

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Table 1: Demographic data of the study

Severity		Number	Mean ± SD
Age	Mild	42	36.595±11.0653
	Moderate	39	48.179±13.6765
	Severe	19	52.579±16.382
Sr choline esterase	Mild	42	1408±433.3596
	Moderate	39	838.949±425.7798
	Severe	19	243.895±141.1646
CRP at admission	Mild	42	8.283±1.6672
	Moderate	39	10.592±1.4333
	Severe	19	14.111±2.2835
CRP 24 hours later	Mild	42	10.221±1.7254
	Moderate	39	15.056±2.5858
	Severe	19	25.579±3.699
CRP 48 hours later	Mild	42	10.255±2.6043
	Moderate	39	17.015±3.1533
	Severe	19	33.942±4.1562
APACHE II score	Mild	42	5.63±1.928
	Moderate	39	13.95±2.781
	Severe	19	26.21+4.008

Table 2: Post-hoc pairwise comparison of variables

Severity			Mean difference	P-value
Age	Mild	Moderate	-11.5842*	0
		Severe	-15.9837*	0
	Moderate	Moderate	11.5842*	0
		Severe	-4.3995	0.462
	Severe	Moderate	15.9837*	0
		Severe	4.3995	0.462
Sr choline esterase	Mild	Moderate	569.0751*	0
		Severe	1164.1291*	0
	Moderate	Mild	-569.0751*	0
		Severe	595.0540*	0
	Severe	Mild	-1164.1291*	0
		Moderate	-595.0540*	0
CRP at admission	Mild	Moderate	-2.3090*	0
		Severe	-5.8272*	0
	Moderate	Moderate	2.3090*	0
		Severe	-3.5182*	0
	Severe	Moderate	5.8272*	0
		Severe	3.5182*	0
CRP 24 hours later	Mild	Moderate	-4.8350*	0
		Severe	-15.3575*	0
	Moderate	Mild	4.8350*	0
		Severe	-10.5225*	0
	Severe	Mild	15.3575*	0
		Moderate	10.5225*	0
CRP 48 hours later	Mild	Moderate	-6.7606*	0
		Severe	-23.6873*	0
	Moderate	Mild	6.7606*	0
		Severe	-16.9267*	0
	Severe	Mild	23.6873*	0
		Moderate	16.9267*	0
APACHE II SCORE	Mild	Moderate	-8.320*	0
		Severe	-20.582*	0
	Moderate	Mild	8.320*	0
		Severe	-12.262*	0
	Severe	Mild	20.582*	0
		Moderate	12.262*	0

Table 3: Distribution of categorical variables based on severity

		Number (%)			P-value
		Mild	Moderate	Severe	
Gender	Female	16(38.10%)	24(61.50%)	9(47.40%)	0.107
	Male	26(61.90%)	15(38.50%)	10(52.60%)	
Neck muscle weakness	Absent	42(100.00%)	5(12.8%)	0	0.001*
	Present	0	34(87.20%)	19(100.00%)	
Ventilator required	No	42(100.00%)	32(82.20%)	0	0.001*
	Yes	0	7(17.90%)	19(100.00%)	
Outcome	alive	42(100.00%)	39(100.00%)	3(15.80%)	0.001*
	expired	0	0	16(84.20%)	

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Table 4: The mortality rate of the variables

	Mortality	
	Alive (N=84)	Expired (N=16)
Age	42.99±14.036	50.25±16.89
Sr choline esterase	1105.24±528.394	228.12±108.628
CRP at admission	9.558333±2.148645	14.1375±2.174052
CRP 24 hours later	12.99643±3.985227	25.675±3.909561
CRP 48 hours later	14.24643±5.863044	33.90625±4.229022
APACHE II SCORE	10.112±5.423	26.812±3.4102

Table 5: Logistic regression analysis of the effect of multiple factors on prognosis

	Beta coefficient	S.E.	Wald	P-value	Odds ratio	95.0% C.I. for Odds ratio	
						Lower	Upper
Sr choline esterase	-0.002	0.004	0.469	0.493	0.998	0.99	1.005
CRP 48 hours later	0.06	0.178	0.114	0.735	1.062	0.749	1.505
APACHE II score	0.365	0.271	1.818	0.178	1.441	0.847	2.45
Age	-0.046	0.054	0.704	0.401	0.955	0.859	1.063
Sex	0.473	1.538	0.095	0.758	1.604	0.079	32.668
Constant	-6.995	5.578	1.572	0.21	0.001	-	-

Table 6: Correlation of variables with severity score

Variables	APACHE II score	
	r value	p-value
CRP at admission	0.79	0.001**
CRP at 24 hours	0.914	0.001**
CRP at 48 hours	0.924	0.001**
Serum choline esterase	-0.742	0.001**

Table 7: Prognostic determination of plasma levels of CRP, S. choline esterase and APACHE II scores using ROC curve

Area under curve	S.E.	Wald	P-value	Asymptotic 95% Confidence Interval ratio	
				Lower	Upper
CRP at admission	0.955	0.02	0.001	0.916	0.995
CRP 24 hours later	0.987	0.013	.001*	0.962	1.012
CRP 48 hours later	1	0	.001*	1	1
APACHE II score	0.986	0.01	.001*	0.966	1.006

DISCUSSION

The present study showed that the CRP levels on admission, 24 h later, and 48 h after AOPP increased according to the severity of AOPP. In addition, the CRP levels in patients with severe AOPP increased over time, while those in patients with mild or moderate AOPP decreased over time. This may be due to the degree of toxicity. Patients with mild or moderate AOPP exhibit reduced acetylcholine stimulation of the cholinergic nerves, stress responses, lesions on organs, and inflammation, leading to relatively low plasma CRP levels.

In contrast, patients with severe AOPP have severe tissue and organ poisoning, multiple organ failure, and severe inflammation, leading to relatively high plasma CRP levels. A previous study demonstrated that AOPP patients have elevated plasma copeptin levels compared with normal subjects and that copeptin levels increase with increasing poisoning severity. In addition, this difference was negatively correlated with acetylcholine esterase levels, an indicator of AOPP severity.

A previous study indicated that the APACHE II score reflects the degree of lesions in organophosphate poisoning, with higher scores indicating a higher risk of respiratory failure. Another study suggested that acetylcholine accumulation in patients with AOPP affects the peripheral cholinergic nerves and inhibits the central nervous system.

Logistic regression analysis in the present study demonstrated that APACHE II scores and acetylcholine esterase levels were high-risk factors for the prognosis of AOPP patients. Kaplan-Meier analysis of the asymptomatic survival curve suggested that patients with plasma CRP levels higher than the median values were more likely to present with other clinical symptoms and reduced treatment efficacy, leading to poorer prognosis.

In addition, ROC analysis in the present study demonstrated that plasma CRP levels and APACHE II score have good sensitivity and specificity for the evaluation of AOPP prognosis. The treatment of AOPP is a clinical challenge for emergency physicians. Active CRP levels, APACHE II scores, evaluation of disease and prognosis, and effective treatment plans are directly associated with patient survival.

CONCLUSION

In conclusion, the present study revealed that changes in CRP and APACHE II scores might be associated with the prediction of AOPP prognosis. Increased levels of C-reactive protein in patients

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with severe acute organophosphorus pesticide poisoning are significant for the prediction of severity and prognosis in patients with acute organophosphorus pesticide poisoning.

Limitations

The present study consisted of a relatively small number of patients and did not investigate the effect of combined cardiovascular, diabetic, liver, or kidney dysfunction on plasma CRP levels and the absence of a control group.

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