



CRP COMPARISON WITH RDW AS A PROGNOSTIC MARKER FOR OUTCOME OF OP POISONING

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ABSTRACT

Background: Organophosphate (OP) compounds are frequently used as pesticides in countries. This ease of availability of the OP compounds has resulted in a gradual increase in unintentional and suicidal poisoning, mainly in developing countries¹. Elevated RDW is associated with systemic inflammation and oxidative stress. More severe poisoning means more production of free radicals and more oxidative stress. In AOPP, toxins may cause lesions in tissues and organs in the body, leading to increased plasma CRP levels^{2,5}. **Aim:** 1-To measure CRP, serum acetylcholinesterase, red cell distribution width, in acute organophosphorus poisoning. 2- To analyze the correlation between these biochemical parameters and serum acetylcholinesterase levels. 3-To analyze the validity of these biochemical parameters in prediction of severity and prognosis in op poisoning. **Methods:** Hospital based prospective study was conducted from OP compound consumption patients attending casualty and admitted patients in S. Nijalingappa Medical College Hospital and Research center, BAGALKOT. Patients less than 18 years, Co-ingestion of organophosphorus with other agents, Pre hospital cardiac arrest, Prior history of Iron deficiency anemia, Vitamin B12 deficiency and folate deficiency anemia, Recent hemorrhage, Chronic liver disease, Prior chemotherapy, Patient on oral contraceptive pills, Patient on estrogen therapy is excluded. **Results:** a total of 60 patients who diagnosed with history of poisoning were involved in the study among them 29 (48.3%) were male and 31 (51.7%) were female. 75% of study population has attempted suicide by taking the poisoning and 10% of study population had accidental consumption of poisoning, and 5% of study population had occupational exposure. **Conclusion:** There is negative correlation between the cholinesterase, RDW and CRP as cholinesterase increases RDW and CRP decreases and severity of poisoning decreases and as cholinesterase decreases RDW and CRP increases and severity of op poisoning increases and morbidity and mortality increases.

KEYWORDS : OP compound poisoning, RDW,CRP, cholinesterase.

INTRODUCTION:

Organophosphate (OP) compounds are frequently used as pesticides in countries, where a great deal of agricultural activities is involved¹. This ease of availability of the OP compounds has resulted in a gradual increase in unintentional and suicidal poisoning, mainly in developing countries¹. The World Health Organization (WHO) has estimated that more than 300 million acute pesticide poisoning occur worldwide each year and most of these cases are due to OP intoxication¹. The mortality rate of acute OP poisoning is 10% – 20% and WHO has estimated that 2,00,000 people die each year from pesticide poisoning¹. OPs cause cholinergic syndrome, which may result in death due to inhibition of the enzymes acetylcholinesterase (AChE) and butyrylcholinesterase (BuChE) or pseudo-cholinesterase (PChE)]. The mortality rate of OP poisoning remains as high as 10-20% despite widely available antidotes used in treatment⁶. Elevated RDW is associated with systemic inflammation and oxidative stress as the exact underlying mechanism is not well understood⁷. Oxidative stress is defined as disturbance of the balance between the production of free radicals and the antioxidant capacity of the body⁷. More severe poisoning means more production of free radicals and more oxidative stress³. Increased oxidative stress contributes to an increase in lipid peroxidation and decrease in the phospholipid content of the erythrocyte membrane. As a result, the erythrocyte membrane is damaged and erythrocytes lose their integrity. The lifespan of mature erythrocytes is shortened⁸. In OP poisoning, there is acute inflammation and increased oxidative stress that can lead to a change in the structure and size of the circulating erythrocyte⁸. Hence, it is expected that RDW levels may be increased in OPI poisoning and can thus aid in prognosis. CRP is an acute phase reactant that can be used for monitoring of infection or autoimmune disease. In patients with such diseases, cytokine, mainly interleukin-6, stimulates the liver cells and promotes the production of CRP. The CRP can be used for the diagnosis and the observation of the

progress of infectious diseases or autoimmune diseases. The concentration of CRP increases in conditions of inflammation, myocardial infarction, stress, trauma, infection, operation and tumor, and is being used to distinguish viral infection from bacterial infection. In AOPP, toxins may cause lesions in tissues and organs in the body, leading to increased plasma CRP levels^{2,5}.

Aims and Objectives of the study:

1. To measure C-reactive protein, serum acetylcholinesterase, red cell distribution width, in acute organophosphorus poisoning.
2. To analyze the correlation between these biochemical parameters and serum acetylcholinesterase levels.
3. To analyze the validity of these biochemical parameters in prediction of severity and prognosis in op poisoning

METHODOLOGY:

Study design:

A case-series study.

Source of study population:

The study will be done on patients who were admitted in S. Nijalingappa medical college and Hanagal shri kumershwara hospital, Navanagar, Bagalkot, between 2020 to 2021

Inclusion Criteria:

All patients aged more than 18 years who are admitted with acute organophosphorus poisoning within 24 hours with clinical features and physical evidence of consumption of the poison irrespective of gender.

Exclusion Criteria:

1. Patients less than 18 years
2. Co-ingestion of organophosphorus with other agents
3. Pre hospital cardiac arrest
4. Prior history of Iron deficiency anemia, Vitamin B12 deficiency and folate deficiency anemia

5. Recent hemorrhage
6. Chronic liver disease
7. Prior chemotherapy
8. Patient on oral contraceptive pills
9. Patient on estrogen therapy

Sample size:

Sample size estimation was done using Medcalc software. At 95% confidence level, and 80% power of the study α (two-tailed) = 0.050 and at 95% confidence level. 80% of power of the study The standard normal deviate for $\alpha = Z\alpha = 1.960$ The standard normal deviate for $\beta = Z\beta = 0.842$ AUC of ROC=0.71, For the RDW in OP cases for clinical outcome³ Sample size estimated is 58=60.

Data collection:

1. after obtaining approval and clearance from the institutional ethical committee, the patient fulfilling the inclusion criteria were enrolled for the study after obtaining informed consent. Total of 60 patient who diagnosed with OP compound poisoning have taken as cases.
2. A questionnaire was used to collect identification data including age, sex, address, occupation, past history, personal history, presenting history, and other comorbidities.

Sample:

venous blood samples (into 2ml of EDTA tube and another 2ml in plain tube) for required blood investigation and other required investigation will be done.

RESULTS:

a total of 60 patients who diagnosed with history of poisoning were involved in the study among them 29 (48.3%) were male and 31 (51.7%) were female ,40% of study population belongs to age group of 21-30 years old and 26% of study population were belongs to age group of 31-40 years. 75% of study population has attempted suicide by taking the poisoning and 10% of study population had accidental consumption of poisoning, and 5% of study population had occupational exposure. chlorpyrifos (31%) was the most commonly used poison. Followed by Monocrotophos constituting about (21%).15 patients were intubated during study period and 5 patients were expired among 60 patients.

- There is negative correlation between the cholinesterase, RDW and CRP as cholinesterase increases RDW and CRP decreases and severity of poisoning decreases.
- As cholinesterase decreases RDW and CRP increases and severity of op poisoning increases and morbidity and mortality increases

Table no 1: Distribution of study population according to various age group

Age in years	No of cases	Percent
≤ 20	13	21.7
21-30	24	40.0
31-40	16	26.7
> 40	7	11.7
Total	60	100.0

Table no 2 : Gender distribution among study population

Gender	No of cases	Percent
Male	29	48.3
Female	31	51.7
Total	60	100.0

Table no 3: Method of consumption of poison among study population

Method of consumption	No of cases	Percent
suicide	45	75.0

occupational exposure	5	8.3
accidental consumption	10	16.7
Total	60	100.0

Table no 4 : poison details among study population

Compound	No of cases	Percent
Bromophos	7	11.7
Chlorpyrifos	19	31.7
Diazinon	8	13.3
Dimethoate	2	3.3
Malathion	7	11.7
Monocrotphos	13	21.7
Quinalphos	4	6.7
Total	60	100.0

Table no 5: Outcome of study population

Outcome	No of cases	Percent
Death	5	8.3
Improved	55	91.7
Total	60	100.0

Table no 6: Respiratory situation among study population

Respiratory situation	No of cases	Percent
Intubated	15	25.0
Not intubated	45	75.0
Total	60	100.0

Table no 7: serum cholinesterase levels among study population

Cholinesterase	Outcome	N	Mean	Std. Deviation	Std. Error Mean	t Value	P Value
Initial	Death	5	526.00	55.95	25.02	4.463	P<0.001
	Improved	55	2677.93	1028.20	138.64		
at 48th hour	Death	5	622.00	213.82	95.62	5.19	P<0.001
	Improved	55	3431.82	1199.74	161.77		

There is statistically significant correlation between acetylcholinesterase value on the day of admission and outcome. Low AChE values are associated with poor prognosis. Hence can be used as a prognostic marker assessment of severity of OP poisoning.

Table no 8 : RDW among study population

RDW	Outcome	N	Mean	Std. Deviation	Std. Error Mean	t Value	P Value
Initial	Death	5	20.60	1.34	0.60	2.787	P<0.007
	Improved	55	17.67	2.30	0.31		
at 48th hour	Death	5	20.80	3.03	1.36	4.508	P<0.001
	Improved	55	15.27	2.59	0.35		

There is statistically significant correlation between red cell distribution width and outcome. Elevated RDW values are a poor prognostic marker. Mean RDW value of around 20.60 is seen in severely ill patients. Ventilator assistance as well as death has statistically significant correlation with elevated RDW value

Table no 9 : CRP among study population

CRP	Outcome	N	Mean	Std. Deviation	Std. Error Mean	t Value	P Value
Initial	Death	5	56.40	19.87	8.89	5.414	P<0.001
	Improved	55	12.80	17.03	2.30		
at 48th hour	Death	5	87.40	29.80	13.33	8.225	P<0.001
	Improved	55	9.98	19.25	2.60		

There is statistically significant correlation between CRP and outcome. Elevated CRP values are a poor prognostic marker.

Mean CRP value of around 56.40 is seen in severely ill patients.

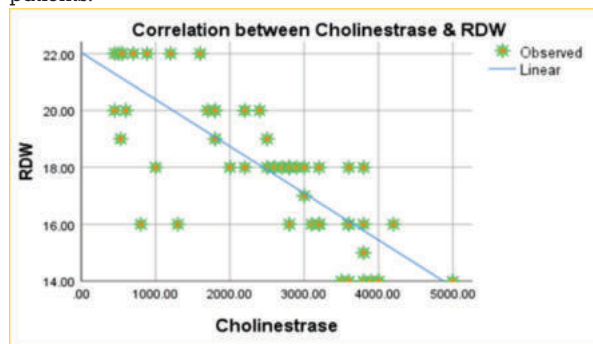


Figure no 1: correlation between cholinesterase and RDW

The above graph shows that there is negative correlation between serum cholinesterase and RDW that is as the cholinesterase value increases the RDW decreases and as the cholinesterase decreases RDW increases

The above figure shows there is negative correlation between cholinesterase and CRP As the cholinesterase increases the CRP decreases and vice versa

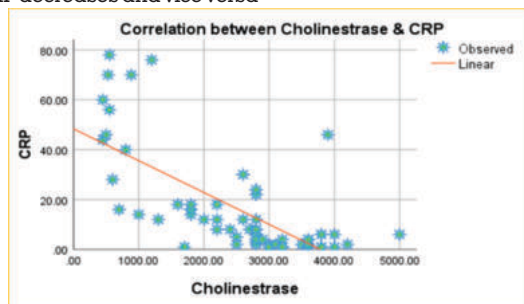


Figure no 2 :- correlation between Cholinesterase and CRP

Table no 10 : validity in comparison to cholinesterase with RDW and CRP

Validity in comparison to Cholinesterase	RDW	CRP
Sensitivity	92%	66%
Specificity	77%	95%
PPV	87.50%	96%
NPV	85%	62%
Diagnostic accuracy	87%	77%

In the above table it shows that RDW has more sensitivity as compared to CRP and CRP has more specificity as compared to RDW, CRP has 96% positive predictive value, RDW has 85% negative predictive value, RDW have 87% diagnostic accuracy, CRP have 77% diagnostic accuracy.

DISCUSSION:

Organophosphate poisoning causes many hematological and biochemical changes on accidental or toxic exposure⁴. It causes increased inflammatory cytokines particularly IL-1b, IL-8 that causes oxidative stress damaging the RBC membranes leading to anisocytosis and elevated RDW⁴. Organophosphate poisoning also reduces certain anti-inflammatory cytokines such as IL-10 further tipping the balance between pro and anti-inflammatory state in the body leading to oxidant damage⁴. The principal oxidant involved is SOD (superoxide dismutase) which damages the RBC membrane by lipid peroxidation of the phospholipid membrane layer releasing Malonyl aldehyde⁴. It also reduces the level of total cholesterol and phospholipid in the RBC membrane making it unstable and prone to sheer stress and alter RBC's shape Also Organophosphates have redox cycling activity, i.e., they accept a free electron and transfer it to O₂ causing free radical generation, thereby oxidant

damage⁴. RBCs are prone to damage easily as they have no nucleus and mitochondria. This makes them easily affected especially during hypoxia which is the feature of Organophosphate poisons. Hypoxia damages the RBC membrane as it leads to auto-oxidation of Hemoglobin (Hb is degraded to methHb) thereby decreasing its oxygen carrying capacity and less affinity with shift of Hb-O₂ dissociation curve to right. This leads to RBC membrane damage and it continues as a vicious cycle until intervened⁴. RDW in OP poisoning further, as estimation of RDW is an inexpensive and utilization of routinely reported data of complete blood count (CBC)¹⁰. C-reactive protein (CRP) is a reactive substance in acute lesions, and elevated plasma levels of CRP are a result of inflammation and trauma. In AOPP, toxins may cause lesions in tissues and organs in the body, leading to increased plasma CRP levels². The levels of CRP 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 toxification. 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. By contrast, patients with severe AOPP have severe poisoning of tissues and organs, multiple organ failure and severe inflammation, leading to relatively high plasma CRP levels².

In our study there were 5 deaths among 60 patients (8.3%) with all of them having elevated RDW and CRP levels both during admission and 48 hours after admission. None died in the RDW and CRP lower group.

CONCLUSION:

Red cell distribution width and CRP are a quick, simple, easy and effective tool to risk stratify Organophosphate poisoning cases in low income, resource poor settings and in most situations where the degree of exposure to poison could not be assessed or wasn't revealed It can be used as an additional tool to predict complications in patients with Organophosphate poisoning and also as a criteria for discharging inpatients who are not at risk of intoxication. Further studies involving larger group of populations representing various cultures and many subsets of populations is needed

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