Red Cell Distribution Width as Outcome Predictor in Organophosphate Poisoning

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I. Background

Suicidal poisoning by OPI is however a major clinical and public health concernRed cell distribution width measures variability in RBC size. That means it reflects anisocytosis. It can easily be assessed in a complete blood count. It is found to be elevated heart failure, acute coronary syndromes and pancreatitis.

In organophosphate poisoning too there can be acute inflammation and oxidative stress. This too may cause a change in structure and size of RBC. So there is an expected increase in red cell distribution width. The level of elevation is associated with the level of inflammation and oxidative stress. Hence RDW can be assessed as a prognostic marker in organophosphate poisoning

Objectives:
To investigate the relation between Red cell distribution width and final outcome in patients with organophosphate poisoning

II. Materials And Methods

The study will be conducted on 200 patients admitted to Government Rajaji Hospital & Madurai Medical College with history of organophosphate poisoning during the study period
We included patients with clinical history of ingestion of OPI poison between age 13- 60 yrs, did initial clinical assessment, serum pseudocholinesterase and RDW

Inclusion Criteria
* Clinical history of ingestion of OPI poison between age 13- 60 yrs

Exclusion Criteria
* Coningestion with other poison
* Prehospital cardiac arrest
* Transfer to another hospital
* Discharge against medical advise
* Coronary artery disease
* Hypertension
* Diabetes
* Abnormal liver function test
* Abnormal renal function test
* Iron deficiency anaemia

DATA COLLECTION:
Informed consent will be obtained from all patients/attenders to be enrolled for the study. In all the patients relevant information will be collected in a predesigned proforma. The patients are selected based on clinical examinations and biochemical tests.

LABORATORY INVESTIGATIONS
a) Complete Hemogram
b) Peripheral blood smear
c) Liver function test
d) Renal function test
e) Random blood sugar
f) PseudoCholinesterase level

Adult patients aged more than 12 years of age attending the casualty of Department of Medicine of Government Rajaji Hospital, Madurai with history of OPC poisoning were admitted. Complete hemogram, blood sugar, urea, creatinine and liver function tests, serum pseudocholinesteraseetc were done. Patients with abnormal blood sugar values, elevated renal function tests and elevated liver function tests were excluded.

DESIGN OF STUDY:
Prospective study

PERIOD OF STUDY:
6 MONTHS

COLLABORATING DEPARTMENTS:
DEPARTMENT OF PATHOLOGY and DEPARTMENT OF BIOCHEMISTRY

ETHICAL CLEARANCE: Obtained
CONSENT: Individualwritten and informed consent.
ANALYSIS: The collected data will be entered in Microsoft Excel spreadsheet and analyzed using Statistical Package for Social Sciences (SPSS) version 17

CONFLICT OF INTEREST: NIL
FINANCIAL SUPPORT: SELF

III. Results

The mean of Systolic Bp, Diastolic Bp, Pulse rate, Respiratory rate, SpO2 and Serum Pseudocholinesterase were measured and shown in Table

RDW	Day 1		Day 3	
	Mean	Std. Deviation	Mean	Std. Deviation
SBP	109.7	30.4	108.2	15.6
DBP	72.9	10.5	79.5	12.1
PULSE RATE	91.4	16.5	80.9	20.1
RESPIRATORY RATE	19.1	5.9	15.0	3.5
SpO2	84.3	11.6	91.5	4.2
Serum Pseudocholinesterase	4200.8	2947.1	5987.4	1208.3

In the RDW higher group there were 7 patients with no adverse effects, 19 who were intubated and extubated early. 46 subjects were intubated and needed prolonged mechanical ventilation beyond 5 days and hence underwent elective tracheostomy. 19 had delayed respiratory failure within 72 hrs requiring mechanical ventilation and 7 died within 30 days in the RDW higher than 46 group.

Outcomes	RDW Low			RDW High		
	No	Yes	Total	No	Yes	Total
No adverse effects	13	89	102	91	7	98
Intubated and early extubated	89	13	102	79	19	98
Intubated needing tracheostomy	102	0	102	52	46	98
Delayed respiratory failure within 72hrs	102	0	102	79	19	98
Death within 30 days	102	0	102	91	7	98

From the t test we derive that the mean serum pseudocholinesterase was lower in RDW high group 1699(SD 1377.6) than the RDW low group 6603.6(SD1841.5) which is statistically significant ($p<0.0001$).
Also the mean SpO2 was lower in the RDW higher group 75.5 (SD 8.8) and higher in RDW 92.7 (SD 6.6) which is also statistically significant ($p<0.0001$).
The mean Respiratory Rate was lower in the RDW higher group 18.2 (SD 5.7) and higher in RDW 20 (SD 6.0) which is also statistically significant ($p<0.030$).
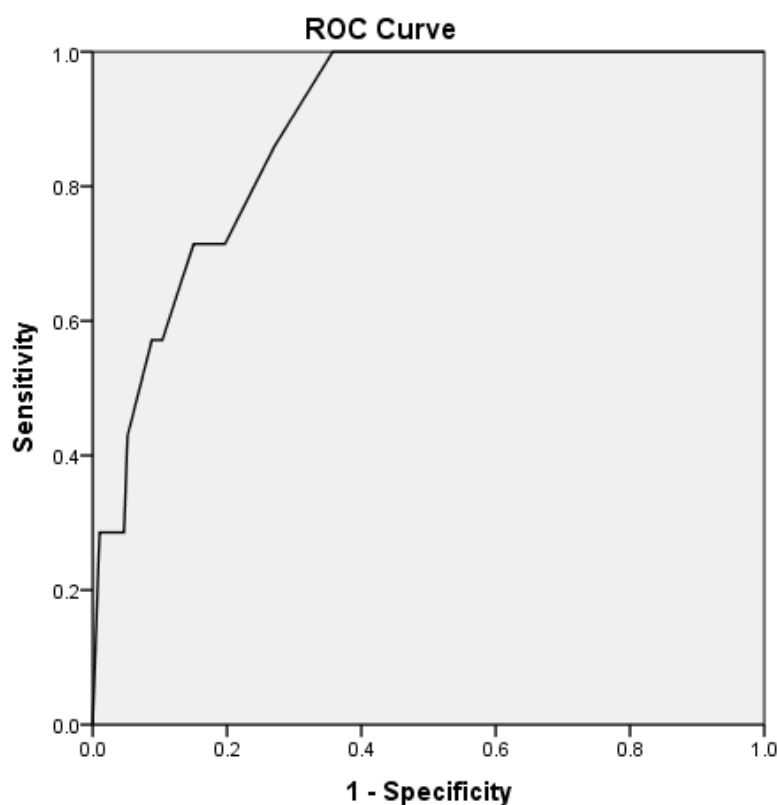
Also the mean Diastolic BP was lower in the RDW higher group 70.4 (SD 11.2) and higher in RDW 75.2 (SD 9.2) which is also statistically significant (p<0.001).

Patients with RDW high than 46 had very low Serum Pseudocholinesterase, Lower SpO2, Diastolic BP and Respiratory Rate which were statistically significant.

RDW	Low		High		P-value
	Mean	Std. Deviation	Mean	Std. Deviation	
Age	36.6	13.1	37.1	12.8	0.792
SBP	107.4	30.7	112.1	30.2	0.283
DBP	75.2	9.2	70.4	11.2	0.001
PULSE RATE	91.1	16.7	91.7	16.3	0.783
RESPIRATORY RATE	20.0	6.0	18.2	5.7	0.030
SpO2	92.7	6.6	75.5	8.8	<0.0001
Serum Pseudocholinesterase	6603.6	1841.5	1699.9	1377.6	<0.0001

ROC (Receiver operating curve) was used to determine the optimal cut off point for RDW for predicting mortality.RDW had a sensitivity of 71.4 % and the specificity of 85 % with a cut-off value of 51.5 in predicting mortality in patients with OPI poisoning. (Area under the Curve: 0.885)

Diagonal segments are produced by ties.

LIMITATION:
* Our study did not involve any intervention.
* The subtype of Organophosphate poison and their outcomes were not studied separately.
* We did not include other types of poison like Carbamate, organochlorines
* We could not quantify the amount of exposure that occurred in each patient
* The height, weight, BMI of patients were not studied, since Organophosphate poisons are fat soluble
* The study had smaller group of population from a Single Institution which may not represent the whole Indian population
* The levels of folic acid, vitamin B12, and iron that might influence the RDW value were not measured

IV. Discussion

Organophosphate poisoning causes many hematological and biochemical changes on accidental or toxic exposure. It causes increased inflammatory cytokines particularly IL-1b, IL-8 that causes oxidative stress damaging the RBC membranes leading to anisocytosis and elevated RDW. 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 damage.

The principle oxidant involved is SOD (superoxide dismutase) which damages the RBC membrane by lipid peroxidation of the phospholipid membrane layer releasing Malonylaldehyde. 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 shapeAlso Organophosphates have redox cycling activity, i.e. they accept a free electron and transfer it to O2 causing free radical generation, thereby oxidant damage.

RBC's 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 intervened.

In our study there were 7 deaths among 200 patients (3.5%) with all of them having elevated RDW levels. None died in the RDW lower group

In study by *Zerrin Define Dundar et al*, 7 (9.7%) died during the intensive care unit follow-up period. The patients who died had higher median RDW levels than survivors [15.40 (15.10-16.40) and 14.30 (13.30-16.00), respectively, p=0.047]

V. Conclusion

Red cell distribution width is 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 in-patients who are not at risk of intoxication.

Further studies involving larger group of populations representing various cultures and many subset of populations is needed

References

[1]. Lippi, G., Targher, G., Montagnana, M. et al, Relationbetween red blood cell distribution width andinflammatory biomarkers in a large cohort ofunselected outpatients. Arch Pathol LabMed. 2009;133:628–632.

[2]. Churi, S., Bhakta, K., Madhan, R. Organophosphatepoisoning: prediction of severity and outcome byGlasgow Coma Scale, poisoning severity score,Acute Physiology and Chronic Health Evaluation IIscore, and Simplified Acute Physiology Score II. JEmergNurs. 2012;38:493–495

[3]. Patel, K.V., Ferrucci, L., Ershler, W.B. et al, Red bloodcell distribution width and the risk of death inmiddle-aged and older adults. Arch InternMed. 2009;169:515–523

[4]. Shaikh Mohammed Aslam ,AkhilaArcotVadivelanRed Cell Distribution Width as Prognostic Markerinorganophosphorous Compound PoisoningIOSR JDMSe-ISSN: 2279-0853, p-ISSN: 2279-0861.Volume 14,Issue 9 Ver. III (Sep. 2015)

[5]. Peter JV, Thomas L, Graham PL, et al. Performance ofclinical scoring systems in acute organophosphatepoisoning. ClinToxicol (Phila) 2013;51:850–4.

[6]. Churi S, Bhakta K, Madhan R. Organophosphatepoisoning: prediction of severity and outcome byGlasgow Coma Scale, poisoning severity score, AcutePhysiology and Chronic Health Evaluation II score, andSimplified Acute Physiology Score II. JEmergNurs2012;38:493–5.