Original Paper

Can Red Cell Distribution Width (RDW) Predict the Mortality in Organophosphorus and Carbamate Insecticide Poisoning?

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ABSTRACT

Organophosphorus (OP) and carbamate (CM) insecticides are among the most toxic of pesticides that cause poisoning in humans, and are the most frequently encountered insecticides in India. They are inhibitors of acetylcholinesterase, OPs acting by irreversibly phosphorylating the enzyme, while CMs reversibly carbamylate it.

Red blood cell distribution width (RDW) is a measure of the variability in size of circulating erythrocytes. It is routinely reported as part of a complete blood count, but its use is generally restricted to narrowing the differential diagnosis of anaemia. Elevated RDW might indicate impaired production or increased destruction of red blood cells, which may reflect unfavourable physiologic conditions that may lead to adverse clinical outcomes. It is well known that RDW levels are affected by various conditions such as erythropoietin stress - during iron, vitamin B12, and folate deficiencies, oxidative stress, thrombocytopenia and inflammatory diseases.

The objective of this study was to explore the possibility of RDW being used as a predictor of mortality in cases of OP and CM poisoning in a South Indian population, free of any pre-existing disease, which may confound the RDW.

Key Words: Organophosphorus insecticide; OP insecticide; Carbamate insecticide; CM insecticide; Acetylcholinesterase; Red blood cell distribution width; RDW

INTRODUCTION

Organophosphorus (OP) and carbamate (CM) insecticide self poisoning is an important health problem in rural regions of the developing world and kills an estimated 2,00,000 people every year.[1] Acute OP and CM poisoning due to intentional self harm exerts a major burden on the health care system and is responsible for greater morbidity and mortality.[2] Hospital based statistics suggests that nearly half of the admissions to the emergency department with acute poisoning are due to OP and CM poisoning.[3] The causes of death in acute poisoning are related to ventricular arrhythmias, CNS depression, seizures or respiratory failure due to excessive bronchial secretions, bronchospasm, pulmonary oedema, aspiration, respiratory muscle paralysis or depression of medullary centre.[4] Late mortality is associated with respiratory failure and infections or complications of mechanical ventilation or intensive care management.[5]

Red cell distribution width (RDW) is a measure of variability in size of circulatory erythrocytes and it plays a role in the differential diagnosis of anaemia.[7] It represents an index of anisocytosis. The two RDW measurements currently in use are the red blood distribution width – coefficient of variation (RDW-CV) and red cell distribution width - standard deviation (RDW-SD). RDW-CV is a calculation based on both the width of the distribution curve and the mean cell size. It is calculated by dividing standard deviation of the mean cell size by the mean corpuscular volume (MCV) of the red cells and multiplying by 100 to convert into percentage, which is

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calculated by division of standard deviation of erythrocyte volume by MCV. The typical reference range spans between 11% and 14%.

Elevated RDW might indicate impaired production or increased destruction of red blood cells, which may reflect unfavourable physiological conditions that may lead to adverse clinical outcomes.[8,9] Recent studies have shown that even within normal range, elevated RDW was closely associated with inflammation, neurohumoral activation, smoking, renal dysfunction, nutritional deficiencies, bone marrow dysfunction, cardiovascular and all cause mortality independent of anaemia.[10,11] Elevated RDW has been shown to predict mortality with great consistency across several different study populations.[12] RDW is an emerging biomarker which is predictive of chronic inflammation, oxidative stress, coronary heart disease etc.[6] Oxidative stress refers to the condition in which the balance between oxidant and antioxidant defenses is upset and excess reactive oxygen species causes oxidative damage to nucleic acids, proteins and lipids. Oxidative stress is related to red cell survival and could be a possible mechanism for RDW.[12]

Since RDW is associated with morbidity and mortality in many debilitating diseases, we hypothesise that RDW may affect the morbidity and/or mortality of patients with organophosphorus and carbamate poisoning.

MATERIALS AND METHODS

Two hundred and eighty seven patients (177 males and 110 females) above the age of 20 years with a history of OP or CM poisoning admitted to RL Jalappa Hospital & Research Centre, Kolar, Karnataka from March 2012 to March 2014 were included in the study **(Table 1)**. A full medical history was obtained. People with pre-existing diseases that could contribute to the morbidity or mortality of the patients, and patients with normal plasma cholinesterase levels were excluded from the study. All patients underwent haematological investigations, including red cell distribution width at the time of hospitalization. RDW is measured as coefficient of variation and is derived from red blood cell distribution curves generated on automated haematology analyzers and is an indicator of variation in red blood cell size within a blood sample. Laboratory normal range for RDW is 11–14%. Based on RDW values, the subjects were grouped as RDW <11%, 11–11.9%, 12–12.9%, 13–13.9% and >14%.

RESULTS

Among the 287 patients studied, 59 died, revealing a mortality of 25.9%. In the study, it was observed that

Table 1: Distribution of subjects according to sex and outcome

		Outcome		Total	χ^2, df, p value
		Death	Survived		
Sex	**Female**	25	85	110	0.514, 1, 0.473
	Male	34	143	177	
Total		59	228	287	

Table 2: Mean differences in age, duration of stay and RDW with respect to outcome

	Outcome	Number	Mean	Standard deviation	t value	p value
Age	Survived	228	31.24	11.060	-2.798	0.005
	Died	59	36.05	14.200		
Duration of stay	Survived	228	7.56	5.281	3.278	0.001
	Died	59	5.14	4.121		
RDW	Survived	228	12.306	1.6157	-4.993	0.000
	Died	59	13.615	2.3722		

there was significant mean difference among survivors and dead subjects with respect to age, duration of stay, and RDW, i.e., mean age was higher, duration of stay was less, and RDW was more among the dead compared to the survivors **(Table 2)**.

In the study, it was observed that there were 177 (61%) males and 110 (39%) females. There was no significant difference in mortality between males and females.

It was observed that there was negative correlation between duration of stay and RDW, i.e., with increase in duration of stay there was decrease in RDW, but there was no significant correlation **(Table 3)**. A significant positive correlation was observed between duration of stay and RDW in survivors, i.e., with increase in duration of stay there was increase in RDW **(Table 3)**.

It was also observed that there was significant association between RDW and outcome, i.e., with increase in RDW there was increase in mortality rate at a significant level **(Table 4)**.

DISCUSSION

To our knowledge, this is the first study to determine the role of RDW in predicting the outcome of patients with OP and CM poisoning. In our study, we evaluated the association of RDW values (obtained during hospitalization) with morbidity and mortality in patients poisoned with OP and CM compounds. We found that RDW apart from providing predictive information on haematological abnormalities was independently associated with mortality and duration of stay (morbidity) of patients with OP and CM poisoning.

Abnormalities in RDW proved to be prognostically meaningful in patients with heart failure due to left ventricular failure or coronary artery disease, etc, mortality in older adults, thrombotic disorders, infection, smoking, etc.[13,14] A strong association between RDW and inflammatory biomarkers was found in a large cohort of adult outpatients.[15] Malnutrition markers, including total cholesterol, are believed to be significantly related to RDW.[16] Renal function, which is a factor linked with malnutrition and inflammation in heart failure, is also associated with RDW values.

Table 3: Correlation between duration of stay and RDW

		RDW	
		Died	**Survived**
Duration of Stay	**Pearson Correlation**	-0.053	0.425**
	Sig (2-tailed)	0.687	0.000
	Number	59	228

Table 4: Correlation between duration of stay and RDW

		Outcome		**Total**	**χ^2, df, p value**
		Died	**Survived**		
RDW	**<11**	8	46	54	24.65, 4, 0.0001
	11–11.9	9	60	69	
	12–12.9	10	61	71	
	13–13.9	12	30	42	
	>14	23	28	51	
Total		59	228	287	

In the present study, we found that mean RDW values of patients who had succumbed to poisoning was significantly greater than mean RDW values of patients who had survived. However the mechanism for association of RDW with outcome of patients with OP and CM poisoning is unclear. The results of our work are expected to contribute to further studies on identifying haematological parameters such as RDW to evaluate the outcome in poisoned patients. Besides monitoring implications, our finding might have therapeutic implications as well because correction of the cause of abnormal RDW values like anaemia, inflammation, etc., in poisoned patients may be of benefit in reducing the morbidity and mortality as is found to be true in cases of heart failure patients.[17]

CONCLUSION

The findings in the present study demonstrate that RDW is independently associated with clinical outcome in OP and CM poisoning patients. Further studies have to be done to validate our results and to make clear the underlying pathophysiology linking RDW with mortality risk in OP and CM poisoning. The mortality and morbidity may be decreased by successful treatment of the underlying disease responsible for raised RDW values.

We suggest that measuring RDW values should be a routine in all OP and CM poisoned patients. Because there is a narrow inter-individual variation in RDW values, even meagre increase in RDW values may be of prognostic significance. Increase in RDW values leads to higher mortality and morbidity in OP and CM poisoned patients.

Along with other parameters, RDW should be considered to identify those patients who have to be triaged and managed aggressively to reduce the mortality in OP and CM poisoned patients.

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