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Red Blood Cell Distribution Width is an Independent Predictor of Mortality in Patients with Carbon Monoxide Poisoning

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Abstract

Introduction: We examined the effect of carbon monoxide (CO) gas, a colourless and odourless product of the incomplete combustion of carbon-based fuels and materials, on red blood cell distribution width (RDW) and investigated whether RDW can be used in clinics when there is no access to carboxyhaemoglobin (COHb) testing.

Methods: We examined 324 patients who presented to our emergency department with CO poisoning during a 2-year period. The age, gender, overall condition, COHb levels, RDW values, symptoms, and outcomes of all patients were recorded.

Results: The mean CO level was 26.8 ± 9.8 and the mean RDW was 14.11 ± 1.4. The most common symptoms were headache (76.5%) and nausea (65.1%). While there was no relationship between the RDW value and gender or outcome (p = 0.532, p = 0.268, respectively), there was a significant correlation between the RDW value and overall condition of patients (p = 0.034).

Conclusions: Since COHb, which is used in the diagnosis of CO poisoning, is not readily available in all settings, we believe that RDW, as a parameter tested during routine complete blood count, can be used to identify high-risk patients.

Keywords: Red blood cell distribution width; Carbon monoxide poisoning; Emergency service; COHb; Carbon monoxide

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Introduction

Carbon monoxide (CO) gas is a colourless, odourless, and tasteless product of the incomplete combustion of carbon-based fuels and substances [1]. It is one of the most common causes of mortality associated with poisoning worldwide. Although CO is naturally present in the body as a by-product of haemoglobin degradation, constituting up to 2% of all haemoglobin, it can enter the body via the exogenous route in cases of incomplete combustion in the environment, resulting in toxicity [2]. The bodily systems most severely affected by CO are the central nervous system (CNS) and cardiovascular system, due to hypoxia. Mortality is largely related to impairment of these two systems [3,4].

Red blood cell distribution width (RDW) provides a measure of the variation in the red blood cell volume/size (anisocytosis) [5-7], and is useful in the following ways [5-9]:

- Elevated RDW is helpful for early detection of nutritional deficiencies, including iron, folate, and vitamin B12 deficiency, where the DRW shows an increase before other red blood cell parameters.
- RDW helps to distinguish uncomplicated iron deficiency anaemia (high RDW, normal or low mean corpuscular volume (MCV)) from uncomplicated heterozygous thalassaemias (normal RDW, low MCV).
- RDW aids in the differentiation of macrocytic (normal RDW) anaemias from megaloblastic anaemias, especially folate or vitamin B12 deficiency-related anaemias (elevated RDW).

Table 1: Vital signs of patients.

Variable	Mean	SD
SBP (mmHg)	129.27	20.1
DBP (mmHg)	76.27	11.8
Pulse (bpm/min)	83.20	12.9
Saturation (%)	92.99	4.8

DBP: Diastolic Blood Pressure; SBP: systolic blood pressure; SD: standard deviation.

- RDW can index marked morphological changes in the context of peripheral smear examinations, because elevated RDW is indicative of the breakdown and agglutination of red blood cells, and of a dimorphic red blood cell population.

The aim of this study was to examine the effect of CO on RDW and to investigate whether RDW has utility in the clinical setting.

Material and Methods

We reviewed 324 patients who presented to our emergency department (ED) with CO poisoning between 1 January 2011 and 31 December 2012. The data were retrieved from the hospital's information system (Synthetic Aperture Real-time Ultrasound System; SARUS) and patient files. The study was approved by the local ethics committee (approval date: 24 July 2013, issue number: 648).

The age, gender, overall condition, vital signs, carboxyhaemoglobin (COHb) levels, RDW values, symptoms, and outcomes of all patients were evaluated. Patients younger than 18 years of age, and those who previously had anaemia or chronic diseases, or no available complete blood count results, were excluded from the study.

The data were analysed using SPSS for Windows software (ver. 19.0; SPSS Inc., Chicago, IL, USA). The Kolmogorov–Smirnov test was used to assess the normality of distribution of the data. Descriptive statistics are provided as means ± standard deviation SD). Chi-square, Student T test was used for group comparisons and $p < 0.05$ was accepted as statistically significant.

Results

The mean age of the 324 cases included in the study was 41.7 ± 16.65 years, and there were 213 (65.7%) female and 111 (34.3%) male patients.

The mean COHb level of the patients was 26.8 ± 9.8% (minimum: 10.1%, maximum: 56.7%) and the mean RDW value was 14.11 ± 1.4.

The mean systolic blood pressure was 129.3 ± 20.2 mmHg, the mean diastolic blood pressure was 76.3 ± 11.9 mmHg, the mean pulse rate was 83.2 ± 13.0 bpm, and the mean oxygen saturation level was 93.0 ± 4.8% (Table 1).

The most common symptom was headache, observed in 248 (76.5%) patients, followed by nausea, observed in 211 (65.1%) patients, and confusion, seen in 143 (44.1%) patients (Table 2).

The mean RDW value of the female patients was 14.1 ± 1.5 and that of the males was 13.8±1.0; there was no difference statistically significant ($p > 0.532$).

Regarding the association between patients' Glasgow Coma Score and RDW shown on the Table 3. There was significant difference in RDW according to Glasgow Coma Score ($p < 0.05$) (Table 3).

Table 2: Frequency of symptoms.

Finding	N	%
Headache	248	76.5
Nausea	211	65.1
Confusion	143	44.1.
Dizziness	112	34.6
Vomiting	105	32.4
Palpitation	50	15.4
Syncope	39	12.0
Altered consciousness	32	9.9
Chest pain	20	6.2
Breathlessness	13	4.0
Abdominal pain	9	2.8
Blurred vision	8	2.5
Seizure	7	2.2
Coma	3	0.9
Asymptomatic	3	0.9

Table 3: The RDW according to Glasgow Coma Score.

	GCS	N	Mean	SD	p
RDW	Good	172	13.9651	1.32442	
	Moderate	112	14.3009	1.44693	0.034
	Poor	40	14.1975	1.15303	
	Total	324			

RDW: Red Blood Cell Distribution Width; SD: Standard Deviation

Table 4: The RDW value by patient outcome.

	Outcome	N	Median	Mean	SD	p
RDW	Discharged from ED	300	160.47	14.0780	1.30860	
	Admitted	20	195.15	14.6550	1.94895	0.268
	Exitus	4	151.38	13.7750	0.66018	
	Total	324				

RDW: Red Blood Cell Distribution Width; SD: Standard Deviation; ED: Emergency Department.

Regarding the association between patient outcomes and RDW, the mean RDW of the 300 patients who were discharged was 14.1 ± 1.3, that of the 20 patients who were admitted to the clinic was 14.6 ± 1.9, and that of the 4 patients who died was 13.8 ± 0.7. There was no significant difference in RDW by patient outcome ($p > 0.05$) (Table 4).

Discussion

Since COHb, which is used in the diagnosis of CO poisoning, is not readily available in all settings, we believe that RDW, as a parameter that is evaluated during routine complete blood count, can be used to identify high-risk patients when there is no access to COHb testing.

In a study done in Turkey by Çiftçi et al. [10], the mean patient age was 27 years, and 55% of the patients were female. In a study by Karabacak et al. [11], the mean patient age was 41 years and 60% were female. In our study, the mean patient age was 41.7 years, and 65.7% of the patients were male. The mean patient age in our study was higher than the average reported in studies done in Turkey and worldwide, predominantly because our hospital does not have an

inpatient ward for paediatric cases, and patients younger than 18 years old might have been referred to other centres. Similar to our study, previous studies have generally reported a female predominance in cases of CO poisoning. In many societies, including our own, men spend their days in the workplaces, which are usually warmed with a central heating system, and spend their evenings in other locations such as cafes, bars, and teahouses. Therefore, men spend relatively less time at home than women. This could explain why women are more frequently affected by CO leaks, which are more likely to occur in the domestic environment.

Carbon monoxide is normally present in living individuals at very low levels. The normal level is 0.5–1.5% in healthy individuals, 3–7% in new-borns, and 4–9% in individuals who smoke. Toxicity symptoms are very obvious at levels of 20–50%, and COHb levels of 50–60% can be fatal. Patients sometimes present with atypical clinical features, such as acute coronary syndrome [12]. The extent of poisoning is directly related to the CO concentration present in the environment and the duration of exposure. Uysalol et al. [13] reported a mean COHb level of 15.54% for their study population. In the present study, the mean COHb level was 26.9%, although some patients had extremely high COHb levels. Considering the half-life of COHb and the time elapsed before presenting to the hospital, it is possible that patients with CO poisoning initially have higher COHb levels than those that are actually measured. Therefore, it is important to carefully consider the symptoms if CO poisoning is suspected, and treatment should be initiated promptly.

Toxicity symptoms usually arise when COHb levels reach 15%, and become profound at levels higher than 20%. COHb levels above 50% are lethal. The most common symptoms when the COHb level is at 10–20% are nausea and fatigue; headache is most common at a level of 20–30%, and dizziness at a level of 30–40%. Rare symptoms include epilepsy and a comatose state, which are observed at high COHb concentrations and have a lethal course [14]. The clinical findings of CO poisoning are non-specific, and often involve the CNS and cardiovascular system. Neurological symptoms, such as headache, drowsiness, dizziness, nausea, and confusion, are detected first, and can be observed even at low COHb levels because neurons are extremely sensitive to this complex [13,15-16]. Sellors et al. [17] reported headache and dizziness as the most common symptoms in patients presenting with acute CO poisoning. Uysalol et al. [13] reported the most frequent symptom as fatigue (61.9%), followed by headache (58.3%). In agreement with the literature, the most commonly observed symptoms in our study were headache and nausea, which are believed to occur due to the extreme sensitivity of CNS to tissue hypoxia.

Many studies have suggested a significant correlation between COHb level and clinical status. Furthermore, studies have shown that CO poisoning causes an anaerobic metabolism at the cellular level, as well as the accumulation of lactic acid [18,19]. Neil et al. [20] and Ilano et al. [21] showed a strong correlation between COHb level and clinical status. Piantadosi [22] reported that although there was a correlation between COHb level and clinical findings, it was not strong, and suggested that COHb levels should not inform any change in the treatment regimen. Meanwhile, it has been reported that hypoxia has detrimental effects on organ systems, and the most severely affected organs are the brain and heart [23]. Low COHb levels in cases of CO poisonings with a fatal course have been attributed to late measurement or an underlying comorbidity (24). COHb has been identified as an important marker for diagnosis and clinical follow-up in cases of acute CO poisoning; however, it has been emphasised that a low COHb level should not rule out a diagnosis of CO poisoning, nor should it be used as the only marker when determining the treatment approach and clinical course [24,25]. In our study, we observed that higher COHb levels were associated with a worse overall condition. In our opinion, the relationship between an increasing concentration of a gas that has such detrimental effects on organ systems and a worsening clinical status appears to be straightforward.

In our review of the literature, we encountered no study reporting an association between RDW and CO poisoning. As a parameter tested during routine complete blood count, RDW indicates the size of circulating red blood cells. RDW is principally used in the diagnosis of anaemia: elevated values indicate haemolysis and/or impaired red blood cell production. In cases of anaemia, RDW starts to increase before MCV decreases [26]. One study tested the assumption that CO poisoning could cause a reduction in RDW values before any reduction in MCV, which is a parameter associated with the oxygen-carrying capacity of blood [27].

Until recently, RDW was considered to be significant only in the context of haematological diseases; however, recent studies have shown that RDW is elevated in various pathologies, and is even directly related to mortality. In particular, elevated RDW levels have been reported in coronary artery diseases [28,29], as well as in heart failure [29,30], pulmonary embolism [31], acute renal failure [32], pulmonary arterial hypertension [33], peripheral artery disease [34], rheumatic diseases [35], and stroke [36]. Since it is associated with so many pathologies, RDW has been studied as a marker of inflammation, and Lippi et al. [37] reported a positive correlation with C-reactive protein levels. RDW has shown an association with mortality in relation to sepsis [38,39], as well as other causes [40]. Majercik et al. [41] studied trauma patients and reported elevated RDW due to progressive inflammation. Marinkovic et al. [42] reported that red blood cell life was shorter in conditions of oxidative stress, which resulted in increased haemolysis and subsequently elevated RDW.

In the present study, RDW levels were elevated in patients with COHb levels between 10% and 20%, although the increase was not marked. ED staff act quicker when the patients have a poor overall condition, both during interventions in the ED and during patient transport. Therefore, it is possible that the blood samples obtained from patients with a poor overall condition were transferred to the laboratory more quickly. Accordingly, a recent increase in RDW in patients with a poor overall condition may not be reflected in the laboratory results. For patients with COHb levels between 10% and 20% in the ED, the most common symptom was headache, which usually develops when COHb levels are around 25%. This suggests that these patients may have had initial COHb levels of between 20% and 30%. For this group of patients, interventions in the ED and blood sampling took longer than for those with a poor overall condition, which could explain why they showed a greater RDW in laboratory results. This might also explain why RDW levels were low in patients with a poor overall condition, and high in those with a moderate condition. Although RDW is not markedly elevated during CO poisoning, in our opinion RDW can increase in control blood samples of CO-poisoned patients due to a shorter lifecycle of red blood cells caused by hypoxic stress and initiation of the inflammatory process. Variation in RDW can be explained by the presence of additional

pathologies underlying acute events, such as acute coronary syndrome and pulmonary embolism, and independent inflammatory processes in rheumatic diseases.

Although there was no significant association between COHb level and RDW in this study, RDW was significantly correlated with patient clinical status. Therefore, in our opinion, when there is no access to COHb testing in cases of suspected CO poisoning, the RDW value can give a further indication to the physician at the ED regarding the patient's clinical status.

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