Role of serum erythropoietin level in evaluating the severity of tissue hypoxia in carbon monoxide intoxicated patients.

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KEYWORDS
Carbon monoxide,
COHb,
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hypoxia.

ABSTRACT

Carbon monoxide (CO) is the second most frequent environmental pollutant worldwide. Tissue hypoxia appears to be the main cause that stands behind the harmful effects of co-poisoning. This study aimed to improve the management of carbon monoxide-intoxicated patients by predicting of use of erythropoietin levels in determining the need for hyperbaric oxygen (HBO) treatment in CO-poisoned patients who were previously categorized as non-HBO needers according to COHB level that was found to be below 25%. This cross-sectional comparative study was carried out on 71 patients presented to the Poison Control Center of Minia University with a history of CO poisoning from 1st February 2020 to April 2022. Arterial blood samples were drawn for carboxyhemoglobin (COHb) level, venous blood samples were drawn on admission and after 2 hours from patients who had COHb < 25 % for erythropoietin (EPO) value, CT and ECG were performed to all patients. We demonstrated that 23 patients had COHb > 25 %, and 48 patients had COHb < 25 %, EPO predicted the need for HBO in 17 patients after 2 hours with a sensitivity of 82.35 % and specificity of 100 %. So we concluded that EPO was a good predictor for the need for HBO in CO-poisoned patients with COHb less than 25%.

Introduction

Carbon monoxide (Co) is a colorless, odorless, nonirritating gas produced by the incomplete burning of any carbonaceous material. It accounts for over half of the fatal poisonings worldwide (Henn et al., 2013).

The severity of poisoning that corresponds with acute CO exposure is often based on nonspecific clinical criteria ranging from headache and confusion to coma and death with the possibility of subsequent neurological and psychiatric sequelae in the survivors (Cho et al., 2008).

Despite the complex patho-physiological cascade of CO Poisoning, tissue hypoxia seems to be the principal causative agent behind the harmful effects of co-poisoning on different body organs (Goldstein 2008).

Carboxyhemoglobin (COHb) measurement is essential for determining exposure to CO, but levels correlate imprecisely with the degree of poisoning and severity of hypoxia. In addition, the measurement of oxygen saturation in CO patients does not represent an accurate measure of hypoxia because CO poisoning

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results in a shift of the oxyhemoglobin dissociation curve to the left (Hampson, 1998).

Indications for the use of hyperbaric oxygen therapy in CO poisoning are neurological findings (coma, focal neurological deficits, altered mental status, and seizures), pregnancy with COHb levels >15%, history of loss of consciousness, cardiovascular compromise (hypotension, ischemia, infarction, dysrhythmia), metabolic acidosis, extremes of age, elevated COHb level (>25%), abnormal neuropsychiatric testing results, concurrent burns, and persistent symptoms despite normobaric oxygen (Kao and Nanagas, 2004 and Goldstein, 2008).

Erythropoietin (EPO) is a glycoprotein hormone synthesized by the proximal convoluted tubules of the kidneys and partially in the liver (10-15% of total production). It was responsible for regulating erythrocytes proliferation, so its production is markedly enhanced by anemia or hypoxia; it is primarily aimed at stimulating RBC production to increase oxygen delivery (Jelkmann and Hellwig-Burgel, 2001).

In this study, we tried to identify tissue hypoxia in CO-poisoned patients by monitoring serum erythropoietin levels away from measuring COHb levels and not being affected by allosteric changes in hemoglobin molecule impairs the unloading of oxygen to tissues despite its availability.

Patients and methods

From February 2020 to March 2022, a cross-sectional comparative study was conducted on 89 patients with CO poisoning presented to the Poison Control Center (PCC) of Minia University hospital.

The present cross-sectional comparative study was applied to 71 patients presented to the PCC of Minia University Hospital with a history of CO poisoning (within the first hour from exposure to CO poisoning) during the period from 1st February 2020 to1st April 2022. We have obtained approval from the Scientific Research Ethics Committee, Faculty of Medicine, Minia University (number: 7:2/2021).

History of exposure to CO was described by the patients themselves or by their relatives and confirmed clinically with manifestations of poisoning, including malaise, nausea, vomiting, dizziness, and headache, together with impaired cognitive function, loss of consciousness, and seizures in more severe cases. Also, history of receiving O_2 in an ambulance or any hospital before arrival at PCC and if blood donation occurred in the last four months was determined.

Since the presenting symptoms and signs are nonspecific, a high suspicion index is needed to avoid misdiagnosis. Further confirmation was done using COHb measurement at the time of presentation before providing any therapeutic measure.

The interpretation of the COHb levels according to Ilano and Raffin (1990) defined the level of COHb > 25% as significantly abnormal, and treatment is mandatory in the form of oxygen therapy, cerebral dehydrating measures, and hyperbaric oxygen therapy.

Study design

After the patients' arrival at PCC, detailed history was obtained, a complete physical examination was performed, and an arterial blood sample was drawn for COHb. If the COHb level is > 25%, the patient referred for receiving hyperbaric oxygen therapy immediately after undergoing a brain CT scan and ECG. While if the COHb level was < 25 %, two venous blood samples were obtained (the first on admission and the second after 2 hours) for serum erythropoietin level, ECG was done. Other venous blood samples were drawn for CBC, liver and renal function tests. Computed Tomography (CT) brain was done after 24 hours.

Patients with COHb < 25% were followed up by repeated ECG and arterial blood gases (ABG). Some patients deteriorated after several hours and were admitted to the intensive care unit (ICU) for artificial ventilation or close observation. They suffered from hypoxia, convulsion, coma, metabolic acidosis, or changes in ECG or CT brain.

Inclusion criteria

Patients arrived at PCC manifested with CO poisoning within the first hour of CO exposure and with COHb levels more than 10 %

Exclusion criteria

Patients with anemia (Hb < 12 g/dl in females and < 14 g/dl in males), active smoking, pregnancy, and history of blood donation in the last four months were excluded as these conditions may lead to a preexisting increase in erythropoietin levels. Patients with renal and liver failure were excluded as these patients may suffer a false decrease in erythropoietin levels. Patients who received O_2 therapy before arrival at PCC were also excluded to avoid the effect of correction of hypoxia on COHB and erythropoietin levels (Haase, 2013).

Catalog No. 21-EPOHU-E01 contains all the necessary reagents required for performing quantitative measurements of (EPO) levels from samples, including serum, plasma, culture medium, or other biological fluids in a sandwich ELISA format. The COHb was measured by an ABG analyzer (Prockop et al., 2007). The erythropoietin was measured by ELISA kit ALPCO at Cutoff point 27mIU/mL (Mossuz et al., 2005).

Statistical analysis

The collected data were coded, tabulated, and statistically analyzed using the SPSS program (Statistical Package for Social Sciences) version 26. Descriptive statistics were done for normally distributed quantitative data by mean, standard deviation (SD), and abnormally distributed quantitative data by Median and Interquartile range (IQR). Analyses were done for continuous data using the Kruskal-Wallis H test and for categorical data using the chi-square test, Pearson's correlation test, Spearman's correlation test, and Mann-Whitney test for nonparametric quantitative data between the two groups. Simple binary Logistic regression analysis was done to evaluate hypoxia and the subsequent need for hyperbaric oxygen. The receiver Operating Characteristics (ROC) Curve was done to calculate the optimal cutoff point, AUC, sensitivity, specificity, PPV, and NPV. The level of significance was taken at (p-value < 0.05).

Results

Minia University Poison Control Center received 89 patients of CO poisoning. Three patients of them suffered from anemia. Eight patients were treated with oxygen in an ambulance before arrival at PCC because six were comatose, and 2 had severe headaches. Seven patients arrived after one hour. The period of patient's admission in PCC ranged between two to fifteen days.

This study included 71 adult patients aged between (19 to 60) years old (30 (42.3%) males and 41 (57.7%) females), and 23 patients had COHb > 25 %. Those who were immediately referred for hyperbaric oxygen therapy, while the remaining 48 patients with COHb < 25 %, were further categorized into HBO therapy seekers and non-seekers according to other indications (Table 1).

Table (1): Comparison between (age, gender) and need for HBO among carbon monoxide-intoxicated patients attending the poison control center (PCC) of Minia University Hospital using the Kruskal-Wallis Test and Pearson Chi-Square Test.

		COHb < 25 %			
		Need HBO	**Not need HBO**	**COHb > 25 %**	**p-value**
Number: n (%)		17 (23.9%)	31 (43.7%)	23 (32.4%)	0.627 (NS)
Mean of age (years)		40.21	34.66	34.70	
Gender n (%)	**Males (30)**	9 (30.0%)	13 (43.3%)	8 (26.7%)	0.516 (NS)
	Females (41)	8 (19.5%)	18 (43.9%)	15 (36.6%)	

n: number, COHb: carboxyhemoglobin, HBO: hyperbaric oxygen, p-value >0.05: Non significant (NS).

Brain CT in patients with COHb > 25 % was accessible in 12 patients, showed hemorrhagic infarction in 3 patients, two patients had Hypodense area of basal ganglia, and six patients had brain edema (Table 2). While in patients who had COHb < 25 %, thirty-one patients were free of any CT or ECG abnormalities and did not require HBO therapy, ten patients needed HBO due to the presence of ECG abnormalities or severe clinical signs as coma or convulsion, two patients had hemorrhagic infarction, one had a hypodense area of basal ganglia, and four had severe brain edema, they also needed HBO (Tables 2, 3, 4 and Figures 1 a, b, c, and d).

Table (2): Comparison between CT findings and need for HBO among carbon monoxide intoxicated patients attending poison control center (PCC) of Minia University hospital by Pearson Chi-Square Test.

CT	COHb < 25 %		**COHb > 25 %**	**Total**	**p-value**
	Need HBO	**Not need HBO**			
Free	10 (18.9%)	31 (58.5%)	12 (22.6%)	53	0.032 (NS)
Hemorrhagic infarction	2 (40%)	0 (0%)	3 (60%)	5	
Hypodense area of basal ganglia	1 (33.3%)	0 (0%)	2 (66.7%)	3	
Brain edema	4 (40%)	0 (0%)	6 (60%)	10	

COHb: carboxyhemoglobin, HBO: hyperbaric oxygen, CT: computed tomography, p-value >0.05: Non significant (NS).

Table (3): Description of convulsion and coma in all carbon monoxide intoxicated patients attending the poison control center (PCC) of Minia University hospital by Pearson Chi-Square Test.

	Convulsion		Coma	
	No	**Yes**	**No**	**Yes**
Number	54	17	46	25
Percent	76.1%	23.9%	64.8%	35.2%

Table (4): Description of ECG in all carbon monoxide intoxicated patients attending poison control center (PCC) of Minia University hospital by Pearson Chi-Square Test.

ECG	COHb < 25 %		COHb > 25 %	Total
	Need HBO	**Not need HBO**		
Normal	2 (3.6%)	31 (55.4%)	23 (41.1)	56
ST segment depression or elevation	15 (100%)	0	0	15

COHb: carboxyhemoglobin

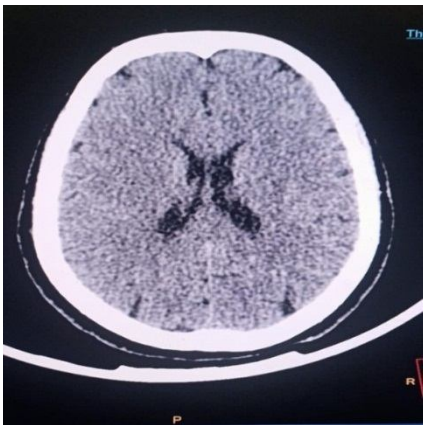
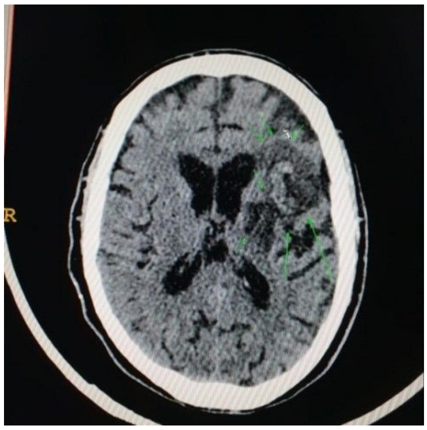
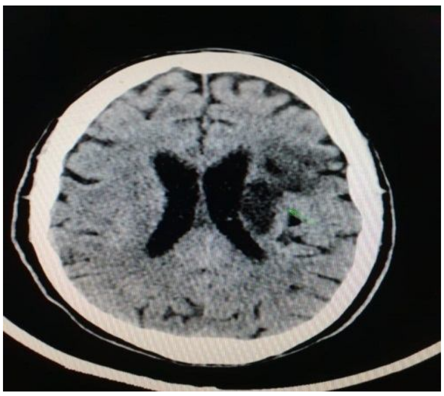


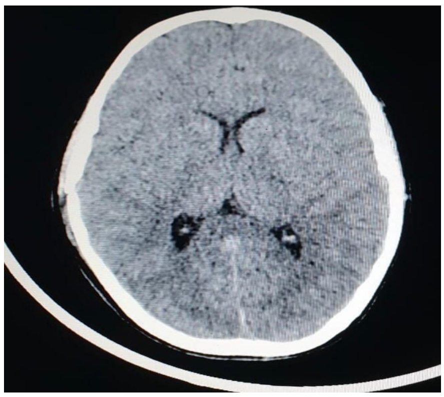
Fig. (1) a", Normal CT brain



"Fig. (1) b", Hemorrhagic infarction "



"Fig. (1) c", Hypodense area of basal ganglia



"Fig. (1) d", Cerebral edema

Fig. (1) Represents a CT scan on the brain of carbon monoxide-intoxicated patients attending the poison control center of Minia University hospital: (a): showed normal brain tissue, (b); showed hemorrhagic infarction, (c); showed hypodense area of basal ganglia and (d); showed cerebral edema.

Pearson's correlation and Spearman's correlation tests in (Table 5) showed an insignificant positive correlation between erythropoietin and age on admission and after two hours (0.158, 0.485 respectively) and between erythropoietin and COHb on admission and after two hours (0.248, 0.077 respectively). However, there was a significant positive correlation between erythropoietin and coma (<0.001*), convulsion (<0.001*), the result of ECG (0.001*), and CT brain (<0.001*) after two hours of admission. The relation between erythropoietin and sex on admission and after two hours was insignificant, as shown in (Table 6).

Table (5): Correlation between erythropoietin and COHb, age, ECG, convulsion, coma, and the result of CT brain in all CO-intoxicated patients using Pearson's correlation and Spearman's correlation

	EPO 0		EPO 2	
	r	**p value**	**r**	**p value**
CO HB 0	0.170	0.248		
CO HB 2			0.258	0.077
Age (P)	0.207	0.158	0.103	0.485
ECG (S)	0.085	0.566	0.466	0.001*
Convulsions (S)	-0.030	0.841	0.558	<0.001*
Coma (S)	0.240	0.100	0.532	<0.001*
CT brain (S)	0.032	0.828	0.598	<0.001*

P: Pearson's correlation, S: Spearman's correlation, and*: Significant level at P value < 0.05, EPO 0: erythropoietin at time of admission, EPO 2: erythropoietin after two hours

Table (6): Relation between erythropoietin and sex in all CO-intoxicated patients by Mann-Whitney test

		Sex		p-value
		Male (n=22)	**Female (n=26)**	
EPO 0	Median	8	14	0.173
	IQR	(5.8-13.3)	(6-18.3)	
EPO 2	Median	16.5	21.5	0.641
	IQR	(8-36.3)	(7-38.3)	

n: number, Mann Whitney test for nonparametric quantitative data between the two groups, the significant level at P value < 0.05, EPO 0: erythropoietin at time of admission, EPO 2: erythropoietin after two hours

As shown in (Table 7), the Simple logistic regression test revealed that erythropoietin level after two hours was a single significant predictor of the need for HBO independent of any other clinical, radiological, or electromechanical predictors. Increasing the erythropoietin level by 0.240 led to an increase in the need for HBO by 1.271. Receiver operating characteristics (ROC) curve analysis detected that sensitivity and specificity of erythropoietin after 2 hours were 82.35% and 100%, respectively (Figure 2).

Table (7): Simple logistic regression analysis to predict the need for HBO by Erythropoietin in carbon monoxide-intoxicated patient on admission and after 2 hours.

	B	Exp (B)	Sig
EPO0	0.046	1.047	0.395 (NS)
EPO2	0.240	1.271	0.001 (HS)

EPO0: erythropiotin on admission, EPO2: erythropiotin after 2 hours, p-value >0.05: Non significant (NS); p-value <0.05: Significant (S); p-value< 0.01: highly significant (HS).

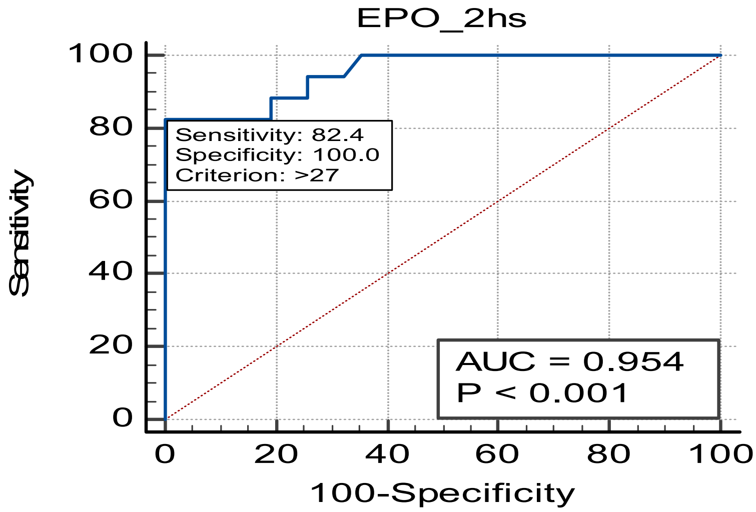


Fig. (2): ROC curve analysis of EPO predicting the need for HBO treatment after 2 hours of admission.

Discussion

Carbon monoxide exerts its harmful effects through tissue asphyxia and inflammatory activity. Tissue asphyxia can be well explained in case of high COHb% more than 25% where CO displaces O_2 from oxygen binding sites on hemoglobin molecules due to the high affinity of hemoglobin to CO, which is 250 times greater than that for oxygen. Therefore, CO rapidly displaces oxygen from binding sites and decreases the O_2-carrying capacity of the blood, resulting in tissue hypoxia (Hampson and Hauff 2008). This theory does not explain tissue asphyxia in patients with low COHb%.

Carbon monoxide induces an allosteric change in hemoglobin molecules that markedly prevents the other three oxygen binding sites from off-loading oxygen at peripheral tissues. Moreover, it impairs cellular respiration by inactivating the reduced cytochrome together with a combination of cardiovascular effects linked to hypoxia, (hypo perfusion or frank ischemia), and intracellular effects, including free radical production and lipid peroxidation. Thus using COHb % alone in identifying patients with tissue asphyxia and subsequently requiring HBO therapy will be inaccurate. Other factors to determine the need for HBO therapy will be necessary (Dubey and Chouksey, 2017).

Treatment with HBO is not based on how high the COHb is. If the COHb is greater than 25%, this is considered severe poisoning, and treatment is justified in agreement with Raub et al.; (2000), so in this study, we classified the patients according to COHb values into patients with COHb more than 25 % referred for HBO, but patients with COHb less than 25 % were classified again according to clinical manifestation and investigation (ECG, brain CT, and clinical manifestations) into HBO therapy seekers and non- seekers.

In this study, there was a significant affection for brain CT in CO-poisoned patients in all groups; this was explained by Lettow et al. (2018) who reported that the mechanism of action of carbon monoxide on the brain was inhibition of oxidative phosphorylation in mitochondria, which led to ischemic injury in the brain, in addition, Carbon monoxide poisoning resulted in the displacement of NO from hemo-containing proteins in platelets and stimulation of guanylate cyclase enzyme which led to increasing brain perfusion and brain edema.

Erythropoietin (EPO) is a glycoprotein hormone responsible for regulating erythrocytes proliferation, so its formation is stimulated by hypoxia; it primarily aims to increase RBC formation to increase oxygen delivery. Its concentration increases after 90–120 min of the reduction of the inspiratory PO2 (Jelkmann and Hellwig-Burgel, 2001).

Tissue hypoxia is the primary stimulus of erythropoietin (EPO) synthesis. The amount of oxygen received by the kidneys and liver is the primary regulator of the production of EPO. Depending on the severity, serum EPO levels increase up to several hundred-folds within minutes: or hours, whereas hyperoxia has the opposite effect (Haase, 2013).

Erythropoietin was a significant indicator for HBO treatment after 2 hours of CO exposure in patients with COHb less than 25 % with sensitivity and specificity (82.35% and 100 % respectively) in agreement with Haase (2013) who reported that the value of EPO was increased in response to hypoxia after 90–120 min.

Coinciding with results published by the Centers for disease control and prevention, the current study showed that ECG changes (ST depression or elevation) were 21.1 %. Neurological abnormalities (convulsion and coma) were 23.9 % and 35.2%, respectively, in agreement with Moon et al. (2010).

The significant positive correlation between erythropoietin and ECG, CT brain, coma, and convulsion coincides with the result published by Henry et al.; (2004) who relieved that hypoxia which may result in coma, convulsion, CT brain changes, or ECG changes stimulate the kidney to secrete erythropoietin.

Conclusion

This study concluded that EPO is sufficient as a single predictor of the need for HBO therapy after 2 hours of CO exposure.

Declaration of Conflicting Interests

The author(s) declared no potential conflicts of interest with respect to the research, authorship, and publication of this article.

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References

Centers for Disease Control and Prevention (CDC) (2007) "Carbon monoxide-related deaths-United States", 1999- 2004. *M.M.W.R. (Morb Mortal Wkly Rep).* 56: p.p. 1309–1312.

Cho, C.H., Chiu, N.C., Ho, C.S. and Peng, C.C. (2008). "Carbon monoxide poisoning in children". *Pediatr Neonatol.* 49: p.p. 121–125.

Dubey, A. and Chouksey, D. (2017). "Carbon monoxide toxicity: A reversible damage to the brain". *Neurol India*. May-Jun; 65(3): p.p. 672-673.

Goldstein M (2008). "Carbon monoxide poisoning". *J. Emerg. Nurs.* 34(6): p.p. 538–542.

Gulati, R., Kwan-Gett, T., Hampson, N., et al. (2009). "Carbon monoxide epidemic among immigrant populations: King County, Washington, 2006". *Am. J. Public Health.* 99(9): p.p. 1687–1692.

Haase, H.V. (2013). "Regulation of erythropoiesis by hypoxia-inducible factors". *Blood Rev.* 27: p.p. 47–53.

Hampson, N.B. (1998). "Pulse oximetry in severe carbon monoxide poisoning". *Chest.* 114(4), p.p. 1036–1041.

Hampson, N.B. and Hauff, N.M. (2008). "Carboxyhemoglobin levels in carbon monoxide poisoning: do they correlate with the clinical picture"? *The American Journal of Emergency Medicine. 26*(6), p.p. 665-669

Henn, S.A., Bell, J.L., Sussell, A.L. and Konda, S. (2013). "Occupational carbon monoxide fatalities in the US from unintentional non-fire related exposures", 1992-2008. *Am. J. Ind. Med.* 56: p.p. 1280–1289.

Henry, D.H., Bowers, P., Romano, M.T. and Provenzano, R. (2004). "Epoetin alfa. clinical evolution of a pleiotropic cytokine". *Arch. Intern. Med.* 164: p.p. 262–276.

Ilano, A.L. and Raffin, T.A. (1990). "Management of carbon monoxide poisoning". *Chest.* 97(1): p.p. 165-169.

Jelkmann, W. and Hellwig-Burgel, T. (2001). "Biology of erythropoietin". *Adv. Exp. Med. Biol.* 502: p.p. 169-187.

Kao, L. and Nanagas, K. (2004). "Carbon monoxide poisoning". *Emerg. Med. Clin. North. Am.* 22(4): p.p. 985-1018.

Kim, H.H. and Choi, S. (2018). "Therapeutic aspects of carbon monoxide in cardiovascular disease". *Int. J. Mol. Sci.*19(8) p.p. 1-12

Lettow, I., Hoffmann, A., Burmeister, H.P. and Toepper, R. (2018). "Delayed neuropsychological sequelae after carbon monoxide poisoning". *Fortschr Neurol Psychiatr.* 86(6): p.p. 342-347.

Moon, J.M., Shin, M.H. and Chun, B.J. (2010). "The value of initial lactate in patients with carbon monoxide intoxication: in the emergency department". *Human and Experimental Toxicology.* 30(8) p.p. 836–843.

Mossuz, P., Girodon, F., Hermouet, S., et al. (2005). "Serum erythropoietin measured by chemiluminescent immunometric assay: An accurate diagnostic test for absolute erythrocytosis". *Clin. Chem*. 51: p.p. 1018–1021

Prockop, L.D., Chichkova, R.I. Prockop, L.D., et al. (2007). "Carbon monoxide intoxication: an updated review". *J. Neurol. Sci.* 262(1-2): p.p. 122-130.

Raub, J.A., Mathieu-Nolf, M., Hampson, N.B. and Thom, S.R. (2000). "Carbon monoxide poisoning-a public health perspective". *Toxicology* 145: p.p. 1–14.

دور نسبة هرمون الأريثروبويتن بالدم في تقييم شدة نقص الاكسجين في مرضى التسمم بغاز أول اكسيد الكربون

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يعتبر أول أكسيد الكربون ثاني أكثر الملوثات البيئية شيوعًا في جميع أنحاء العالم. يبدو أن نقص الأكسجة في الأنسجة هو السبب الرئيسي وراء الآثار الضارة للتسمم بأول أكسيد الكربون. لذا تهدف هذه الدراسة إلى التنبؤ باستخدام مستوى الإريثروبويتين في تحديد الحاجة إلى العلاج بالأكسجين عالي الضغط في المرضى المصابين بالتسمم بأول أكسيد الكربون والذين تم تصنيفهم سابقًا على أنهم بحاجة إلى أكسجين عالي الضغط وفقًا لمستوى الكربوكسي هيموغلوبين الذي وجد أنه أقل من ٢٥٪. أجريت هذه الدراسة على ٧١ مريضاً تم تقديمهم إلى مركز مراقبة السموم بجامعة المنيا ولديهم تاريخ من التسمم بأول أكسيد الكربون خلال الفترة من الأول من فبراير ٢٠٢٠ إلى الأول من أبريل ٢٠٢٢. تم سحب عينات الدم الوريدي عند الوصول وبعد ساعتين للمرضى الذين لديهم كربوكسي هيموغلوبين <٢٥٪ لقيمة إرثروبويتين ، تم إجراء أشعة مقطعية للمخ وتخطيط القلب الكهربائي لجميع المرضى. وأظهرت النتائج أن ٢٣ مريضاً لديهم كربوكسي هيموغلوبين > ٢٥٪ و ٤٨ مريضاً لديهم كربوكسي هيموغلوبين <٢٥٪ ، الإريثروبيوتين تنبأ بالحاجة للأكسجين عالي الضغط في ١٧ مريضاً منهم بعد ساعتين بحساسية ٨٢,٣٥٪ ونوعية ١٠٠٪. نستخلص من هذا أن الإريثروبيوتين مؤشراً جيداً للحاجة إلى الأكسجين عالي الضغط في المرضى المصابين بالتسمم بأول أكسيد الكربون والذين لديهم كربوكسي هيموغلوبين أقل من ٢٥٪.