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Cardiological aspects of carbon monoxide poisoning

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Abstract: Aim: The aim of this study was to assess cardiological manifestations of carbon monoxide (CO) poisoning.
Background/introduction: Carbon monoxide intoxication is one of the most important toxicological causes of morbidity and mortality worldwide. Early clinical manifestation of CO poisoning is cardiotoxicity.
Materials and methods: We enrolled 75 patients (34 males and 41 females, mean age 37.6 ± 17.7 y/o) hospitalized due to CO poisoning. Laboratory tests including troponin I, blood pressure measurements, HR and electrocardiograms (ECG) were collected. Pach's scale scoring and grading system was used to establish severity of poisoning.
Results: Grade of poisoning is positively correlated with troponin I levels and systolic blood pressure. Moreover, troponin levels are significantly correlated with exposition time, lactates and are higher in tachycardiac, hypertensive and positive ECG subpopulations. COHb levels are indicative of exposure but do not correlate with grade of poisoning. The main cause of CO poisoning were bathroom heaters — 83%, only 11% of examined intoxicated population were equipped with CO detectors.
Conclusions: Complex cardiological screening covering troponin levels, ECG, blood pressure and heart rate measurements as well as complete blood count with particular attention to platelet parameters

should be performed in each case where CO intoxication is suspected. More emphasis on education on CO poisoning is needed.

Key words: carbon monoxide poisoning, CO intoxication, clinical toxicology, CO cardiotoxicity, troponin elevation, myocardial injury.

Introduction

Carbon monoxide (CO) poisoning is the most common gas intoxication. It remains one of the most important toxicological causes of morbidity and mortality. Yearly incidence of CO poisoning, based on emergency department visits in United States is around 50.000, 16 per 100.000 [1]. During the 2015/16 winter season the Headquarters of the State Fire Service of Poland reported 3878 incidents of CO poisoning, 2229 CO poisoning victims and 50 CO related deaths. These figures are probably the tip of the iceberg because of the underdetection and underreporting of CO poisoning [2]. Proper diagnosis can be easily missed as the signs and symptoms associated with carbon monoxide poisoning are vague, nonspecific and variable even if the condition is a life-threatening medical emergency.

CO is responsible for tissue hypoxia by forming carboxyhaemoglobin and shifting the oxyhamoglobin dissociation curve leftward [3]. CO affinity to haemoglobin is around 210–250 times greater than that of oxygen [4], which is why even small amounts of CO are impairing oxygen binding and thus reduce oxygen carrying capacity. Furthermore CO binds to ferrous heme proteins, including myoglobin in heart, mitochondrial cytochrome c oxidase (CCO) and more. CCO inhibition results in slowing down oxidative phosphorylation and impairing mitochondrial function. CO also causes inflammation by increasing levels of cytosolic heme and the heme oxygenase-1 (HO-1) protein, resulting in intracellular oxidative stress. In addition CO causes platelet activation and neutrophil degranulation, involving the release of myeloperoxidase (MPO), proteases, and reactive oxygen species which cause oxidative stress, intensified inflammatory cascade, lipid peroxidation and apoptosis [5].

CO is called “silent killer” due to its physical properties such as poisonousness, colorlessness, odorlessness and tastelessness. Clinical manifestations of CO poisoning are nonspecific and might be vague. The diagnosis is established based on carboxyhaemoglobin level (%COHB), evidence of exposure and clinical symptoms. The importance of early and proper recognition of clinical manifestations is essential.

Acute CO poisoning poses a significant threat especially to the central nervous system and heart. Neurologic sequelae are well described in literature. Cardiological manifestations are of interest lately, but not much data is provided. For that reason we aimed to assess cardiological parameters in the group of subjects suffering from

acute CO poisoning, which may be useful to appropriately diagnose, asses the severity of poisoning and consequently implement early treatment with prevention of unfavorable short and long-term negative effects.

Materials and methods

Participants

For our single-center observational study we enrolled 75 patients (34 males and 41 females, mean age 37.6 ± 17.7 y/o) hospitalized in the Toxicology Clinic, Department of Toxicology and Environmental Diseases, Jagiellonian University Medical College due to CO poisoning. Laboratory tests, initial physical examination and electrocardiograms were performed at admission to the hospital. Full interview with poisoned patients, extended clinical evaluation, Pach's scale scoring and grading of poisoning were conducted during 2nd ± 1 day of hospitalization. A diagnosis of CO intoxication was made according to medical history and COHb level >5% in non-smoking and COHb >10% in smoking population. Patients' COHb levels were obtained by spectrophotometric method using the CO-Oximeter AVL 912 analyzer (Roche, Basel, Switzerland). Exposition time was defined as approximate time of CO inhalation based on medical interview and emergency records. Electrocardiograms were assessed by cardiologist. Criteria for defining myocardial ischaemia were ST elevation, or ST depression with T wave changes according to *Third universal definition of myocardial infarction — experts consensus* [6]. Exclusion criteria included underlying cardiovascular diseases, chronic hepatic diseases, dialysis due to chronic kidney failure, malignancy. Participants were fully informed of the study details and gave their written consent. The study protocol was approved by the Jagiellonian University Bioethics Committee, approval no: KBET/172/B/2013. All the procedures complied with the Declaration of Helsinki.

Methods

We assessed grade of CO poisoning using specific Pach's scale which comprises of five parameters: age, exposition time, %COHb, lactates concentration and severity of intoxication (Pach score) depending on state of consciousness and presence of other neurological symptoms. The poisoning grade from I (mild) to III (severe) is then established by summing up obtained points (Table 1) [7].

Statistics

Continuous variables are presented as mean ± standard deviation (SD) or median and interquartile range, depending on the normality of distribution. The normality

Table 1. Pach's scale of poisoning — Pach's CO intoxication grading system. Poisoning grade: I° mild: 1–4 points, II° medium: 5–8 points, III° severe: ≥9 points; COHb — carboxyhaemoglobin.

Parameter	Points-score			
	0	1	2	3
Age (years)	<29	30–39	40–49	>50
Exposition time(min)	<30	31–60	61–120	>120
Pach score	I	II	III	IV
COHb (%)	neg.	<15%	15–30%	>30%
Lactates (mmol/l)	1.0–1.78	1.8–3.6	3.7–5.4	>5.5

of distribution was tested using the Shapiro-Wilk test. Comparisons between the groups of patients were made by the independent samples t-test, or the Mann-Whitney U-test depending on the normality of distribution. One-way ANOVA or respectively Kruskal-Wallis tests were used for statistical analysis of differences between grades of three Pach's groups of poisoned patients. The correlation was evaluated by Spearman's correlation test. To assess changes between two categorical variables we used chi-squared test. In the cases of 2 × 2 contingency tables Yates correction was applied. All p-values are two-sided, $p < 0.05$ was considered statistically significant. Calculations were performed using Statistica 12 (StatSoft® Inc. USA).

Results

Median CO exposition time was 30 min (15–62 min). Majority of hospitalized patients — 83% live in a city, 17% in the countryside. Main cause of CO poisoning were bathroom heaters — 83%. 49% of the study group had lost consciousness, 51% did not. Only 11% of the examined intoxicated population were equipped with CO detectors. Trauma was reported in 17% of cases. 25% of the studied population admitted to being chronic smokers. Baseline characteristics of study groups are presented in Table 2. Troponin levels are strongly positively correlated with grade of poisoning. Furthermore systolic blood pressure and estimated mean arterial pressure is associated with higher grade of poisoning. We found positive correlation with the number of platelets and severity of poisoning according to Pach's grading system. However mean platelet volume (MPV), platelet distribution width (PDW) and ratio of large platelets P-LCR are significantly negatively correlated with poisoning grade as shown in Table 2.

Table 2. Baseline characteristics of study patients. Grade of poisoning is established according to Pach's CO intoxication grading system. Spearman correlations coefficients and significance levels between grade of poisoning and selected parameters are presented additionally.

Parameter		Grade of poisoning			P ANOVA	Rho Spearman	P Spearman
	N = 75 100%	I mild 45.9%	II medium 37.7%	III severe 16.4%			
Age (years)	30 (23–51)	23 (20–28.5)	40 (30–63)	51.5 (44–67)	0.000	0.62	0.000
Exposition time (min)	30 (15–62)	20 (15–30)	60 (15–180)	120 (25–300)	0.011	0.39	0.002
COHb (%)	22.47.7	20.8 ± 7.2	22.1 ± 7.0	25.7 ± 11.3	0.444		0.249
Lactates (mmol/l)	2.1 (1.5–3.1)	1.8 (1.4–2.7)	2.3 (1.9–2.9)	4.9 (2.7–5.9)	0.008	0.43	0.002
HR (min^{-1})	84.5 (80–100)	84 (76–100)	83 (80–100)	100 (80–110)	0.499		0.248
SBP (mmHg)	130 (117–130)	130 (110–130)	130 (120–145)	130 (130–150)	0.029	0.35	0.007
DBP (mmHg)	80 (70–80)	80 (70–80)	80 (70–80)	80 (80–80)	0.755		0.458
eMAP (mmHg)	113.3 (100.0–116.7)	113.3 (98.3–116.7)	113.3 (106.7–123.3)	113.3 (113.3–130.0)	0.106	0.28	0.033
TnI (μg/l)	0.001 (0.001–0.020)	0.001 (0.001–0.001)	0.001 (0.001–0.050)	0.050 (0.001–0.420)	0.003	0.51	0.000
SpO2 (%)	99.0 (98.0–99.6)	99.0 (98.3–99.0)	98.5 (98.0–99.0)	99.0 (93.4–100.0)	0.671		0.617
Glc (mmol/l)	6.0 (5.0–6.9)	6.4 (5.0–6.8)	5.9 (4.8–7.8)	5.4 (5.0–7.5)	0.959		0.825
Na (mmol/l)	140.4 ± 2.6	140.1 ± 2.5	140.9 ± 2.6	139.6 ± 4.1	0.562		0.434
K (mmol/l)	4.2 ± 0.4	4.2 ± 0.5	4.3 ± 0.3	4.3 ± 0.6	0.399		0.268
WBC (10^9/l)	7.9 ± 3.0	8.2 ± 2.7	7.5 ± 2.4	7.9 ± 1.6	0.694		0.852
RBC (10^{12}/l)	4.6 ± 0.5	4.7 ± 0.4	4.6 ± 0.4	4.1 ± 0.8	0.257		0.203
HGB (g/l)	13.5 ± 1.7	13.8 ± 1.6	13.4 ± 1.8	12.9 ± 2.2	0.669		0.283
HCT (%)	39.9 ± 4.1	40.7 ± 3.5	39.8 ± 4.5	37.8 ± 6.0	0.547		0.247
MCV (fl)	87.4 ± 5.8	86.2 ± 4.6	85.9 ± 6.8	93.1 ± 4.6	0.017		0.119
MCH	29.6 ± 2.5	29.2 ± 2.4	28.9 ± 2.8	31.6 ± 1.6	0.065		0.414
MCHC (mmol/l)	33.8 ± 1.2	33.8 ± 1.4	33.6 ± 1.0	34.0 ± 1.2	0.753		0.643

Table 2. Cont.

Parameter		Grade of poisoning			P ANOVA	Rho Spearman	P Spearman
	N = 75 100%	I mild 45.9%	II medium 37.7%	III severe 16.4%			
PLT (10^9/L)	219.0 (188.5–263.0)	219.0 (194.0–252.0)	238.5 (208.0–292.0)	257.0 (196.0–368.0)	0.416	0.30	0.048
RDW-CW (%)	13.3 ± 1.1	13.5 ± 1.0	13.6 ± 1.1	13.6 ± 1.4	0.946		0.530
RDW-SD (fl)	52.6 ± 65.9	41.6 ± 3.1	41.9 ± 3.5	45.6 ± 5.9	0.328		0.132
MPV (fl)	11.1 ± 1.1	11.4 ± 1.1	11.1 ± 0.9	10.1 ± 1.1	0.139	–0.48	0.008
PCT (%)	0.2 (0.2–0.3)	0.2 (0.2–0.3)	0.3 (0.2–0.3)	0.3 (0.2–0.4)	0.665		0.169
PDW (fl)	13.8 ± 2.5	14.6 ± 2.6	14.0 ± 2.5	11.8 ± 2.1	0.097	–0.44	0.016
P-LCR (%)	33.8 ± 8.7	36.3 ± 8.7	34.1 ± 7.6	26.5 ± 9.2	0.188	–0.44	0.014

Abbreviations: COHb — carboxyhemoglobin, HR — heart rate, SBP — systolic blood pressure, DBP — diastolic blood pressure, eMAP — estimated mean arterial pressure, TnI — troponin I, SpO2 — pulse oximeter oxygen saturation, Glc — glucose level, Na — natrium level, K — potassium level, WBC — white blood cell count, RBC — red blood cell count, HGB — hemoglobin, HCT — hematocrit, MCV — mean cell volume, MCH — mean cell hemoglobin, MCHC — mean cell hemoglobin concentration, PLT — platelet count, RDW — relative distribution width of red blood cells by volume, MPV — mean platelet volume, PCT — platelet crit, PDW — platelet distribution width, P-LCR — ratio of large platelets — defined as the percentage of platelets with a size of more than 12 fL.

Table 3. Spearman correlation coefficients for cardiological parameters. All the variables from Table 2 were examined and only significant correlations are shown.

Parameter		Rho Spearman	p
TnI	Age	0.41	0.001
	Exposition time	0.29	0.027
	SBP-DBP	0.37	0.007
	Lactates	0.29	0.038
	Grade of poisoning	0.51	<0.001
HR	Exposition time	0.32	0.020
SBP	Age	0.52	<0.001
	K	0.31	0.027
	HCT	0.33	0.018

Abbreviations: TnI — troponin I, SBP — systolic blood pressure, DBP — diastolic blood pressure, HR — heart rate, K — potassium level, HCT — hematocrit.

CK, CK-MB and NT-pro BNP were not routinely collected in the study, nevertheless we found no correlation between troponin I and available CK, CK-MB and NT-pro BNP measures.

Table 4. Significant differences in examined cardiac parameters between different subpopulations of patients.

Dependent variable	Independent variable	P (MWU test)
TnI	Hypertension	0.003
	Tachycardia	<0.001
	Consciousness disturbances	0.011
	ECG myocardial injury	<0.000001
SBP	IHD	0.002

IHD — history of ischaemic heart disease, HT — hypertension, ECG — electrocardiogram, MWU — Mann-Whitney U test.

ECG findings suggesting myocardial ischaemia were found in 13.3% of study population. We observed significant differences between grade of poisoning, occurrence of tachycardia and systolic hypertension compared to incidence of ECG ischaemia changes (Fig. 1). We observed no correlation between positive acute ischaemic ECG findings along with sex, augmented % COHb and smoking.

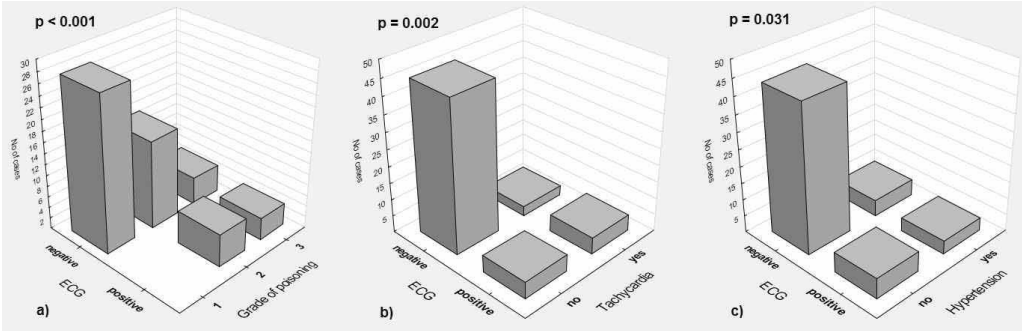

Fig. 1. Bivariate histograms of eloectrocardiographic (ECG) myocardial ischaemia changes versus a) grade of poisoning, b) tachycardia, c) hypertension. P values calculated using chi-squared test with Yates correction when applicable.

Discussion

CO poisoning is the most common gaseous intoxication. Carbon monoxide leads to tissue hypoxia by numerous mechanisms. Indirectly, by connecting with the heme related proteins such as hemoglobin, inhibiting oxygen release [8]. Directly, by binding with the cytochrome C-oxydase and myoglobin causing oxidative stress and destruction of exposed cells and tissues [9]. Cardiac and brain tissue are the most sensitive to CO — caused hypoxia.

Neurologic short — term and long — term aspects of CO intoxication are well described. Cardiological sequelae are of interest recently, but still not much data is provided. Thus we aimed to assess fundamental cardiological parameters in the group of CO intoxicated patients, hospitalized for that reason.

CO intoxication diagnosis is established traditionally after confirmation of history of CO exposure, presence of symptoms consistent with CO poisoning and elevated levels of carboxyhemoglobin (COHb) [10]. COHb is also frequently used as a predictor of severity of intoxication [11]. However, increasing number of evidence states that changes of blood COHb do not correlate with clinical presentation [12]. Accordingly, our study confirmed that elevated COHb levels are indicative of exposure but do not correlate with grade of poisoning. This is explained by various factors influencing CO washout time [13]. Probably improvement of peak CO haemoglobin measurement with the use of handheld pulse CO oximeters would result in more precise results better correlated with subsequent signs and symptoms and thus improve treatment decision-making process. Further investigation of COHb levels or other intoxication prognostic parameters are needed.

As mentioned, heart is one of the most affected organs after acute CO intoxication. Profound cardiovascular CO toxic effects influence electrical, functional, and morphological changes in cardiac tissue. Troponins are widely available and specific biomarkers of myocardial injury. High troponin levels predict long-term mortality in numerous diseases such as coronary artery disease [14], pulmonary embolism [15], diabetes [16], renal failure [17], critical illness [18] and more. In our study group troponin levels are significantly correlated with grade of poisoning, exposition time and pulse pressure (SBP — DBP). Myocardial injury represented by elevated troponin levels is an independent short-term [9] and long-term mortality predictor [19] in CO poisoned patients. This altogether leads to the conclusion that troponins are a useful screening tool in predicting clinical severity and effects of CO intoxication and should be measured on regular basis when CO poisoning is suspected.

Hypoxia leads to tachypnoea that results in a higher rate of inhaled carbon monoxide, ischaemia and subsequent tachycardia. Heart rate and exposition time are positively correlated. Thus, heart rate, especially with tachycardia, may be a useful tool in establishing exposition time, which is often unknown. Furthermore, systolic blood

pressure measured at the admission to the hospital increases together with the severity of poisoning. However, this compensatory mechanism may result in hypotonic state and cardiovascular collapse [20] which was not observed in our study group.

CO poisoning may increase the risk of arrhythmias, notably due to free radicals expression [21]. The most common electrographic disturbance is the disruption of repolarization and prolongation of the QT interval [22]. Electrocardiographic manifestations of myocardial injury following CO intoxication are common especially when impaired consciousness or hypertension are observed [23]. Troponin I levels were significantly elevated in hypertensive, tachycardiac and myocardial injury ECG positive subpopulations as well as the group with consciousness disturbances. These findings may suggest that complex basic early cardiological assessment covering biochemical: troponin, electrical: ECG and clinical: heart rate, blood pressure and state of consciousness, parameters may play a role in diagnosis and prediction of severity of intoxication. Undoubtedly, more attention should be paid to abovementioned multipart cardiological diagnostic performed as early as possible [24].

The data concerning the predictive role of lactate levels in CO poisoning patients provide conflicting results [25, 26]. Cervellin *et al.* stated that lactate levels may be useful tools in predicting severity of CO intoxication, and are well correlated with troponin levels [27]. We confirmed abovementioned findings.

The impact of CO intoxication on thrombosis formation is vague and ambiguous. We found that platelet count was positively correlated with severity of poisoning. This may result in increased thromboembolic formation, which was described lately in CO intoxicated patients [28], and be an additive effect in short and long-term morbidity due to cardiac reasons. Furthermore, recent studies imply that other platelet indices such as medium platelet volume (MPV), platelet distribution width (PDW) and platelet large cell ratio (P-LCR) might be valuable as prognostic factors to assess outcomes in coronary artery disease and acute coronary syndromes [29, 30]. In early stages of CO poisoning lowering of these parameters may be caused by reactive inflammatory platelet formation with consumption of large, hyperactive platelets at the sites of ongoing thrombus formation [19]. Larger platelets have higher expression of glycoprotein Ib and IIb/IIIa receptors and release more thromboxane A2, thus aggregate more quickly [12]. Consequently, potential subsequent changes in platelet parameters in CO intoxication process should be thoroughly investigated.

Moreover, one issue should alarm the authorities: majority of the study group consisted of young people intoxicated by bathroom heaters. The minority of them was supplied with CO detectors. More preventive measures including education and consequently supplementation of CO sensor should be implemented.

In summary, cardiological manifestations of CO poisoning are common, but sometimes not obvious. Troponin levels, heart rate, and systolic blood pressure correlate with exposition time or grade of poisoning. Therefore, we recommend that

complex cardiological screening covering troponin levels, ECG, blood pressure and heart rate measurements as well as complete blood count with particular attention on platelet parameters should be performed in each case when CO intoxication is suspected. Analysis of these parameters would help determine the severity of intoxication and may add valuable prognostic information about CO poisoning, consequently improving implementation of proper treatment and thus short and long-term outcomes.

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References

1. *Hampson N.B.*: Emergency department visits for carbon monoxide poisoning in the Pacific Northwest. J Emerg Med. 1998 Oct; 16 (5): 695–698.
2. *Iqbal S., Clower J.H., Boehmer T.K., Yip F.Y., Garbe P.*: Carbon monoxide-related hospitalizations in the U.S.: evaluation of a web-based query system for public health surveillance. Public Health Rep Wash DC 1974. 2010 Jun; 125 (3): 423–432.
3. *Ernst A., Zibrak J.D.*: Carbon monoxide poisoning. N Engl J Med. 1998; 339 (22): 1603–1608.
4. *Piantadosi C.*: Diagnosis and treatment of carbon monoxide poisoning. Resp Care Clin North Am. 1999, 5: 183–202.
5. *Thom S.R., Bhopale V.M., Han S.-T., Clark J.M., Hardy K.R.*: Intravascular neutrophil activation due to carbon monoxide poisoning. Am J Respir Crit Care Med. 2006 Dec 1; 174 (11): 1239–1248.
6. *Thygesen K., Alpert J.S., Jaffe A.S., et al.*: Third universal definition of myocardial infarction. Eur Heart J. 2012 Oct 2; 33 (20): 2551–2567.
7. *Pach J., Persson H., Sancewicz-Pach K., Groszek B.*: Comparison between the poisoning severity score and specific grading scales used at the Department of Clinical Toxicology in Krakow. Przegl Lek. 1999; 56 (6): 401–408.
8. *Garg J., Krishnamoorthy P., Palaniswamy C., et al.*: Cardiovascular Abnormalities in Carbon Monoxide Poisoning: Am J Ther. 2014 Feb; 1.
9. *Kao H.-K., Lien T.-C., Kou Y.R., Wang J.-H.*: Assessment of myocardial injury in the emergency department independently predicts the short-term poor outcome in patients with severe carbon monoxide poisoning receiving mechanical ventilation and hyperbaric oxygen therapy. Pulm Pharmacol Ther. 2009 Dec; 22 (6): 473–477.
10. *Weaver L.K.*: Carbon monoxide poisoning. N Engl J Med. 2009; 360 (12): 1217–1225.
11. *Kaya H., Coşkun A., Beton O., et al.*: COHgb levels predict the long-term development of acute myocardial infarction in CO poisoning. Am J Emerg Med. 2016 May; 34 (5): 840–844.
12. *Hampson N.B., Hauff N.M.*: Carboxyhemoglobin levels in carbon monoxide poisoning: do they correlate with the clinical picture? Am J Emerg Med. 2008 Jul; 26 (6): 665–669.
13. *Bruce M.C., Bruce E.N.*: Analysis of factors that influence rates of carbon monoxide uptake, distribution, and washout from blood and extravascular tissues using a multicompartment model. J Appl Physiol Bethesda Md 1985. 2006 Apr; 100 (4): 1171–1180.
14. *Omland T., Pfeffer M.A., Solomon S.D., et al.*: Prognostic value of cardiac troponin I measured with a highly sensitive assay in patients with stable coronary artery disease. J Am Coll Cardiol. 2013 Mar 26; 61 (12): 1240–1249.

15. *Kilinc G., Dogan O.T., Berk S., Epozturk K., Ozsahin S.L., Akkurt I.*: Significance of serum cardiac troponin I levels in pulmonary embolism. J Thorac Dis. 2012 Dec; 4 (6): 588–593.
16. *Hallén J., Johansen O.E., Birkeland K.I., et al.*: Determinants and prognostic implications of cardiac troponin T measured by a sensitive assay in type 2 diabetes mellitus. Cardiovasc Diabetol. 2010 Sep 15; 9: 52.
17. *Apple F.S., Murakami M.M., Pearce L.A., Herzog C.A.*: Predictive value of cardiac troponin I and T for subsequent death in end-stage renal disease. Circulation. 2002 Dec 3; 106 (23): 2941–2945.
18. *Lim W., Qushmaq I., Devereaux P.J., et al.*: Elevated Cardiac Troponin Measurements in Critically Ill Patients. Arch Intern Med. 2006 Dec 11; 166 (22): 2446–2454.
19. *Henry C.R., Satran D., Lindgren B., Adkinson C., Nicholson C.I., Henry T.D.*: Myocardial injury and long-term mortality following moderate to severe carbon monoxide poisoning. Jama. 2006; 295 (4): 398–402.
20. *Meyer G., André L., Kleindienst A., et al.*: Carbon monoxide increases inducible NOS expression that mediates CO-induced myocardial damage during ischemia-reperfusion. Am J Physiol Heart Circ Physiol. 2015 Apr 1; 308 (7): H759–767.
21. *André L., Gouzi F., Thireau J., et al.*: Carbon monoxide exposure enhances arrhythmia after cardiac stress: involvement of oxidative stress. Basic Res Cardiol. 2011 Nov; 106 (6): 1235–1246.
22. *Macmillan C.S., Wildsmith J.A., Hamilton W.F.*: Reversible increase in QT dispersion during carbon monoxide poisoning. Acta Anaesthesiol Scand. 2001 Mar; 45 (3): 396–397.
23. *Satran D., Henry C.R., Adkinson C., Nicholson C.I., Bracha Y., Henry T.D.*: Cardiovascular Manifestations of Moderate to Severe Carbon Monoxide Poisoning. J Am Coll Cardiol. 2005 May; 45 (9): 1513–1516.
24. *Kalay N., Ozdogru I., Cetinkaya Y., et al.*: Cardiovascular Effects of Carbon Monoxide Poisoning. Am J Cardiol. 2007 Feb; 99 (3): 322–324.
25. *Doğan N.Ö., Savrun A., Levent S., et al.*: Can initial lactate levels predict the severity of unintentional carbon monoxide poisoning? Hum Exp Toxicol. 2015 Mar; 34 (3): 324–329.
26. *Benaissa M.L., Mégarbane B., Borron S.W., Baud F.J.*: Is elevated plasma lactate a useful marker in the evaluation of pure carbon monoxide poisoning? Intensive Care Med. 2003 Aug; 29 (8): 1372–1375.
27. *Cervellin G., Comelli I., Rastelli G., Picanza A., Lippi G.*: Initial blood lactate correlates with carboxyhemoglobin and clinical severity in carbon monoxide poisoned patients. Clin Biochem. 2014 Dec; 47 (18): 298–301.
28. *Karabacak M., Varol E., Turkdogan K.A., Duman A., Akpinar O., Karabacak P.*: Mean Platelet Volume in Patients With Carbon Monoxide Poisoning. Angiology. 2014 Mar 1; 65 (3): 252–256.
29. *Celik T., Kaya M.G., Akpek M., et al.*: Predictive Value of Admission Platelet Volume Indices for In-hospital Major Adverse Cardiovascular Events in Acute ST-Segment Elevation Myocardial Infarction. Angiology. 2015 Feb 1; 66 (2): 155–162.
30. *Sarli B., Baktir A.O., Saglam H., Arinc H., Kurtul S., Sivgin S., et al.*: Mean platelet volume is associated with poor postinterventional myocardial blush grade in patients with ST-segment elevation myocardial infarction. Coron Artery Dis. 2013 Jun; 24 (4): 285–289.