British Journal of Medicine & Medical Research
17(12): 1-7, 2016, Article no.BJMMR.25824
ISSN: 2231-0614, NLM ID: 101570965

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Early Detection of Cardiac Affection in Acute Carbon Monoxide Intoxicated Patients

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Authors' contributions

This work was carried out in collaboration between all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/BJMMR/2016/25824
Editor(s):
(1) Chan-Min Liu, School of Life Science, Xuzhou Normal University, Xuzhou City, China.
(2) Salomone Di Saverio, Emergency Surgery Unit, Department of General and Transplant Surgery, S. Orsola Malpighi University Hospital, Bologna, Italy.
Reviewers:
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(6) Romeu R. de Souza, São Judas Tadeu University and São Paulo University, Brazil.
Complete Peer review History: http://www.sciencedomain.org/review-history/16306

Original Research Article

Received 22nd March 2016
Accepted 10th September 2016
Published 23rd September 2016

ABSTRACT

Background and Objective: Cardiovascular sequelae of Carbon monoxide (CO) poisoning may be clinically occult and remains undiagnosed due to lack of overt symptoms as acute chest pain and ischemic changes in the ECG. The advent of more sensitive and specific markers capable of detecting minor degree of cardiac damage may enable the clinicians to detect patients suffering from acute CO cardiotoxicity. The main objective of this study is to detect the cardiac effects of carbon monoxide toxicity through the estimation of cardiac biomarkers.
Subjects and Methods: An observational prospective study design was used in the data collection process. Cardiovascular system examination and Electrocardiography (ECG) were performed for eighty CO poisoned patients who reported to Poison Control Center (PCC), Ain

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Shams university Hospital, Egypt over six months. Patients with coronary artery disease or other known heart disease, patients with renal failure as well as smoker subjects were excluded. Carboxyhemoglobin level (COHb), serial cardiac markers (serum of aspartate aminotransferase (AST), creatine kinase-MB (CPK-MB), lactate dehydrogenase (LDH), and cardiac troponin-I (cTnI) quantitative determination) have been assessed.

Results: ECG changes were present in 67.7% of patients. cTnI was 100% sensitive and 73.2% specific, CPK-MB was 79.5% sensitive and 92.7% specific, LDH was 69.2% sensitive and 92.6% specific while AST was 71.8% sensitive and 73.2% specific. cTnI was found elevated in 43 out of 80 cases. There was no statistical significant difference between cardiac markers in patients with normal and changed ECG. There was no statistical significant difference between COHb in patients with normal and elevated cTnI.

Conclusion: Although CO poisoned patients may present to the PCC, fully conscious, with low COHb level, even with free ECG recordings, yet the possibility of cardiac affection should not be excluded. This highlights the importance of cTnI detection in the serum of CO poisoned patients even those with normal ECG recordings to detect any minute cardiac injury.

Keywords: Carbon monoxide poisoning; cardio toxicity; cardiac markers; cardiac troponin-I.

1. INTRODUCTION

Nowadays Carbon monoxide poisoning is one of the most common occupational risk factors leading to various heart diseases [1]. Continuous exposure to CO can lead to myocardial infarction, life-threatening dysrhythmias, and cardiac arrest [2]. In volunteers with low-level exposures (COHb 24%) a decreased exercise tolerance and signs and symptoms of myocardial ischemia was observed. Acute mortality from CO usually results from ventricular dysrhythmias, probably predominantly caused by the accompanying hypoxia [3].

On continuous exposure of CO several patterns of ECG alterations have been observed. These changes may be quickly reversible, delayed or prolonged. Repolarization abnormalities such as: Elevated ST segment, abnormal Q wave, QT interval prolongation have been observed after acute CO poisoning [4].

Myocardial injury may exist in children with CO poisoning without abnormal ECG findings. Glasgow Coma Scale (GCS), score ≤ 14 and hypotension were associate factors with myocardial injury [5].

LDH is found in skeletal muscle as well as in the liver, heart, kidneys and red blood cells. Its use for the detection of myocardial injury is declining as it is not cardiospecific [6].

Myoglobin is an oxygen binding protein of cardiac and skeletal muscles [7].

Although CK-MB is specific for the myocardium, yet it is found approximately 1% in normal skeletal muscle. Therefore CK –MB elevations may be noticed in severe skeletal muscle injury following trauma or surgery or even multiple organ failure. The later may occur in patients with severe CO poisoning and can lead to absolute elevations of CK-MB by less than 1% of the total CK activity [8].

Earlier AST determination was used for the diagnosis of a heart attack, or myocardial infarction. AST can assist in determining and extent of a recent myocardial infarction, although it is less specific than CK-MB, myoglobin, troponin and LDH [9]. Although Myocardial injuries such as angina or pericarditis do not increase AST levels [10].

Cardiac troponin, a myocardial protein has three protein subunits C, T and I. cardiac protein T and I (cTn T and cTn I) have higher sensitivity and specificity in indicating minor myocardial injury [11-12]. Any damage or injury to the myocardial cells results in release of cardiac troponins into the blood circulation. Which can be detected by troponin assay [13-15].

The cardiac specific antibodies used in these assays do not cross-react with the skeletal muscle isoforms of troponin [16-17].

Elevated serum troponin I and cardiac enzymes indicates cardiac affection in CO poisoned cases [18-20].

The main objective of this study is to detect the cardiac effects of carbon monoxide toxicity through the estimation of cardiac biomarkers. Also to detect the changes observed in ECG of patients reported with CO toxicity.

2. SUBJECTS AND METHODS

This study was designed after collecting data of CO poisoned patients. Cardiovascular system examination and Electrocardiography (ECG) were performed for eighty CO poisoned male patients who reported to Poison Control Center (PCC), Ain Shams university Hospital, Egypt in 2008 after taking ethical approval. They were observed for 6 months. Patients with coronary artery disease or other known heart disease, gastrointestinal, respiratory, renal disorders as well as smoker subjects were excluded. All cases with acute CO poisoning were subjected to full medical history and clinical examination.

2.1 Methodology

Method for AST: Methods for the determination of serum AST (SGOT) include ultraviolet kinetic analysis and colorimetric methods. The present method is based on a modification of the colorimetric method by Doumas and Briggs which offers increased specificity and shortened incubation time.

Method for Tn I: TnT concentrations were assayed by a commercially available automated two-site immunoassay (Stratus Cardiac Troponin I; Baxter Dade, Milano, Italy) that includes two monoclonal antibodies specific for cardiac isotype of the protein. The measuring range of the method was from 0.35 (analytical sensitivity declared by the manufacturer) to 50 j.tg/L, the assay generating Tn! results within 10 mm.

Total CK Activity: The catalytic concentration of CK was determined according to the method recommended by the IFCC [21] at 37 #{176}C (Bracco, Milano, Italy). The decisonal concentrations for AIvII used in this study were >160 U/L for women and >190 U/L for men.

CK-MB: The mass concentration of CK-MB was measured with a commercially available immunoabsorbant assay (Stratus CKMB; Baxter Dade) with a sensitivity of 0.4 g/L. The discriminator value for AMI was 5 j.tg/L and 2.5 for the relative index [CK-MB (.tg/L)/total CK (U/L)] X 100].

Myoglobin: The serum myoglobin concentration was assayed with the immunological latex method (Istituto Behring; Scoppito, L'Aquila, Italy), and a discriminator value for AM! of 50 j.tg/L was chosen.

2.2 Statistical Analysis

Statistical analyses were carried out using the SPSS® software package, version 15.0 (SPSS Inc., Chicago, IL, USA) for Windows®. Numerical variables are shown as mean ± SD, and qualitative variables are shown as number and percentage. The χ^2-test and Pearson's correlation test (r) were used to determine differences between qualitative variables. A P-value of < 0.05 was considered to be statistically significant.

Sensitivity and specificity tests were done which are defined as:

- Sensitivity : is the proportion of positives that are correctly identified by the test.
- Specificity: is the proportion of negatives that are correctly identified by the test.

3. RESULTS

As per Table 1, there was no statistical significant difference observed between cardiac markers in patients with normal and changed ECG.

Table 2 showed that, the sensitivity of CPK- MB was high (79.5%) i.e. (79.5%) of CO poisoned patients with ECG changes had elevated serum CPK-MB, while the specificity was very high (92.7%) i.e. (92.7%) of those with normal ECG recordings have normal serum level of CPK-MB.

Table 1. Cardiac markers in relation to ECG recordings in the studied acute CO poisoned patients

Cardiac markers	Normal ECG (No. = 41)	ECG changes (No. = 39)	Probability
	Mean±SD	Mean±SD	P
(cTnI) (ng / ml)	1.34±0.9	1.57±0.9	*P*=0.26
CPK- MB (IU/L)	44.2±28.7	47.3±31	*P*=0.79
LDH(IU/L)	333.9±70.5	330.9±74.5	*P*=0.84
AST(IU/L)	54.5±49.8	59.8±40.4	*P*=0.28

P>0.05 = Non signifiant; No.: Number of cases; SD: Standard deviation

Table 2. Sensitivity, specificity and diagnostic accuracy of serum CPK-MB , LDH, AST, cardiac troponin I (cTnI)in relation to ECG recordings in the studied acute CO poisoned cases

Cardiac marker	Normal ECG (No.= 41)		ECG changes (No. = 39)		Sensitivity	Specificity	Diagnostic accuracy
	Number	%	Number	%			
Normal CPK-MB (No. =46)	38	92.7	8	20.5			
Elevated CPK-MB (No. =34)	3	7.3	31	79.5	79.5%	92.7%	86.3%
Normal LDH (No. =30)	38	92.7	12	30.8	69.2%	92.6%	81.3%
Elevated LDH (No. =30)	3	7.3	27	69.2			
NormalAST (No. =41)	30	73.2	11	28.2	71.8%	73.2%	72.5%
Elevated AST (No. =29)	11	26.8	28	71.8			
Normalcardiac troponin(cTnI) (No. = 30)	30	73.2	0	0	100%	73.2%	86.3%
Elevatedcardictroponin I (cTnI) (No. = 50)	11	26.8	39	100			

*No.: Number of cases; *: Significant at P ≤ 0.05*

The diagnostic accuracy was high (86.3%). There was a statistical significant association between LDH and ECG changes. The sensitivity of LDH was high (69.2%) i.e. (69.2%) of CO poisoned patients with ECG changes had elevated serum LDH, while the specificity was very high (92.6%) i.e. (92.6%) of those with normal ECG recordings have normal serum level of LDH. The diagnostic accuracy was high (81.3%). There was a statistical significant association between AST and ECG changes. The sensitivity of AST was high (71.8%) i.e. (71.8%) of CO poisoned patients with ECG changes had elevated serum AST. while specificity of AST was high (73.2%) i.e. (73.2%) of those with normal ECG recordings have normal serum level AST. The diagnostic accuracy was high (72.5%). There was a statistical significant association between Troponin I level and ECG changes. The sensitivity of Troponin I was very high (100%) i.e. all CO poisoned patients with changes recorded by ECG had elevated troponin I (cTnI) serum level while, the specificity was high (73.2%) i.e. (73.2%) of those with normal ECG recordings have normal serum level of troponin I (cTnI). The diagnostic accuracy was high (86.3%). When a correlation test was done for Troponin I level with CO intoxicated patients, r^2 was found to be 0.89 which indicates that TnI level is changed when the level of CO in blood increases.

Table 3 showed that, there was statistical significant difference between the means of AST,LDH, CPK-MB and cTnI serum levels in patients with delay times less than or more than 5 hours. Patients with delay time more than 5 hours showed statistical significant higher means of AST, LDH, CPK-MB and cTnI serum levels than in patients with delay time less than 5 hours.

Table 3. Cardiac markers and its relation to the delay time in CO poisoned cases

Delay time / Investigation	Less than 5 hours (No. = 55)	More than 5 hours (No. = 25)	Probability
	Mean± SD	Mean± SD	P
AST(IU/L)	38.88±45.8	59.4±44.9	*P*=0.04
LDH(IU/L)	344.5±68	303.4±75.4	*P*=0.01
CPK-MB(IU/L)	42.5±27.4	83.9±33.9	*P*=0.10
cTnI (ng / ml)	1.1±0.9	3.5±0.5	*P*=0.03

**: Significant at P ≤ 0.05; SD: Standard deviation; No.: Number of cases*

Table 4 showed that, there was no statistical significant difference between the mean COHb% in patients with normal and elevated cardiac troponin I There was no statistical significant difference between GCS in patients with normal and elevated cardiac troponinI.

Table 5 showed that, 12 patients with elevated cardiac troponinI (cTnI) treated in the observation room, 8 patients with elevated cardiac troponinI (cTnI) were admitted to inpatient unit, and 23 of them were admitted to ICU. There was no statistical significant association between site of admission and cardiac troponin I level.

4. DISCUSSION

The sensitivity and specificity of cardiac markers in relation to ECG recordings in diagnosing CO cardiotoxicity were also were assessed in the current study. The results revealed that, CPK-MB sensitivity was (79.5%) while the specificity was very high (92.7%). There was a statistical significant association between CPK- MB and ECG changes. The diagnostic accuracy was high (86.3%). For LDH, there was a statistical significant association between LDH and ECG changes. The sensitivity of LDH was high (69.2%), while the specificity was very high (92.6%). The diagnostic accuracy was high (81.3%). There was a statistical significant association between AST and ECG changes. Both the sensitivity of AST (71.8%) and specificity (73.2%) were high. The diagnostic accuracy was high (72.5%). There was a statistical significant association between cTnI level and ECG changes. The sensitivity of cTnI was very high (100%) while, the specificity was high (73.2%). The diagnostic accuracy was high (86.3%). By comparing the sensitivity of the different cardiac markers, cTnI was the most sensitive (100%), followed by CPK-MB (79.5%) then AST (71.8%) and finally LDH (69.2%). When a correlation test was done for Troponin I level with CO intoxicated patients, r^2 was found to be 0.89 which indicates that TnI level is changed when the level of CO in blood increases. Though no significant changes were observed in the ECG of CO intoxicated patients. Thus this study reveals that Cardiac damage is produced by CO intoxication without clinical symptoms.

The above observations were agreed with those of **Mair,** who stated that, patients with normal CPK-MB levels and elevated cTnI levels could be attributed to the low sensitivity and specificity of CPK-MB in detecting areas with microinfarction [21].

It further agreed with **Collinson, Ross, Wilcox, Carlson, Lata, Kontos, Kontos** stated that, development of immunoassays for cardiac troponins (cTnI and cTnT) had enhanced the diagnostic specificity. Measuring of cTnI was completely specific for cardiac damage, allowing quantitation of the extent of infarction and was diagnostically superior to CPK-MB measurement [22-28].

Our study highlights the importance of cTnI detection in the serum of CO poisoned patients, even those with normal ECG recordings to detect any minute cardiac injury.

Table 4. Cardiac troponin I (cTnI) in relation to COHb and GCS level in the studied acute CO poisoned patients

Cardiac troponin I (cTnI)	Normal (cTnI) (No. = 37)	Elevated (cTnI) (No. = 43)	Probability
COHb%	**Mean± SD**	**Mean± SD**	**P**
	24.8±11.9	21.9±13.1	*P*=0.27
GCS	10.7±3.7	9.1±4.1	*P*=0.10

No.: Number of cases; SD: Standard deviation; P>0.05 = Non signifiant

Table 5. Cardiac troponin I (cTnI) in relation to the sites of admission in the studied acute CO poisoned patients

Cardiac troponin I (cTnI)	Normal (cTnI) (No. = 37)		Elevated (cTnI) (No. = 43)		*P*-value
Site of admission	**Number**	**%**	**Number**	**%**	
Observation (n = 27)	15	40.5	12	27.9	
Inpatient (n = 18)	10	27	8	18.6	0.167
ICU (n = 35)	12	32.4	23	53.5	

No.: Number of cases; SD: Standard deviation; P>0.05 = Non signifiant

5. CONCLUSION

Although CO poisoned patients may present fully conscious, with low COHb level, may be treated in the observation room and discharged, do not require ICU admission or even with free ECG recordings, yet the possibility of cardiac affection should not be excluded. This highlights the importance of cTnI detection in the serum of the CO poisoned patients even those with normal ECG recordings to pick up any minute cardiac injury. So cTnI should be routinely measured in all CO poisoned cases.

CONSENT

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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Peer-review history:
The peer review history for this paper can be accessed here:
http://sciencedomain.org/review-history/16306