Assessment of Exposure To Carbon Monoxide Poisoning and Oxidative Stress in Egyptian Patients

Protocol of thesis

Submitted for partial fulfillment of master degree in environmental science

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List of Abbreviations

ABG	Arterial blood gas
AGE	Advanced glycation end-products
ALE	Advanced lipoxidation end-products
ANP	Atrial natriuretic peptide
AST	Aspartate amino transferase
BNP	Brain natriuretic peptide
CAD	Coronary artery disease
cGMP	Cyclic guanosine monophosphate
CO	Carbon monoxide
COHb	Carboxyhemoglobin
CK-MB	Creatine phosphokinase myocardial band
CK-MM	Creatine phosphokinase myocardial muscle
CK-BB	Creatine phosphokinase brain band
CNS	Central Nervous System
cTnI	Cardiac troponin I
cTnT	Cardiac troponin T
DNS	Delayed neuropsychiatric sequelae
ECG	Electrocardiogram
HBOT	Hyperbaric oxygen therapy
HF	Heart failure
HO	Hemeoxygenase
LDH	Lactate dehydrogenase
LOC	loss of conscious
LV	left ventricle

LVEF	left ventricle efficacy
MBP	Myelin basic protein
MDA	Malondialdehyde
mEq/L	milliequivalent/Litre
mg	milligram
mg/dl	milligram/deciliter
mmHg	millimeter mercury
NBO	normobaric oxygen
NO	Nitric oxide
NOS	Nitric oxide synthetase
NT-ProBNP	N-terminal prohormone of brain natriuretic
Pcc	Poison Control Center
Pss	Poisoning severity score
ROS	Reactive oxygen species
SD	Standard deviation
SGOT	glutamic oxaloacetic transaminase
TAC	Total Antioxidant Capacity

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ABSTRACT

Background:

Myocardial injury is a frequent consequence of carbon monoxide (CO) poisoning. Oxidative stress affection seems to be a relevant mechanism in the patho-physiology of patients with acute CO poisoning.

Methodology:

This study included Sixty two CO intoxicated patients who were admitted to Poison Control Center, Ain Shams university Hospitals, between Jan 2007-june 2008.We have investigated some plasma oxidative stress parameters of individual exposed to CO, including Total Antioxidant Capacity (TAC), malondialdehyde (MDA) and nitric oxide (NO).Cardiac muscles damage assessed by determining the serum levels of some cardiac markers as aspartate amino transferase(AST), Total creatine phosphoknase(CPK), creatine kinase-MB(CPK-MB), Lactate dehydrogenase(LDH), troponin I and N-terminal prohormone of brain natriuretic peptide (NT-ProBNP).In addition to carboxyhemoglobin (COHb) levels and Blood pH were also determined to give an indication on the severity of CO exposure. All the investigated parameters were also conducted to 15 healthy individuals who were considered as control group.

Results:

As expected, compared to control group, the patients groups mild and severe showed a significant increase in plasma level of COHb level,oxidative stress parameters, MDA and NO were also increased along with the cardiac markers troponin I, NT-Pro BNP peptide. On the other hand ,there was a sharp reduction in blood pH and Total antioxidant capacity(TAC), NT-Pro BNP showed a significant positive correlation with COHb level and a negative correlation with TAC, while TAC showed a significant negative correlation with COHb level.

Conclusions and recommendations:

Myocardial injury is frequently accompanied with patients of CO poisoning. The oxidative stress indices are significantly affected after CO poisoning .In general it's suggested natural products with antioxidative activity may help to relieve the clinical symptoms of patients who get exposed to CO. The recommendation is to include antioxidant as a supplemented therapeutic strategy along with hyperbaric oxygen treatment which is expected to relieve the clinical symptoms of CO intoxicated patients.

Keywords: Carbon monoxide; Cardiotoxicity; Oxidative stress; troponin I; NT-ProBNP; CPK; CPK-MB; MDA; NO

INTRODUCTION

In the USA, each year 40,000 patients are hospitalized with carbon monoxide (CO) poisoning with reported death rates from 0% to 31%.CO poisoning is the most common cause of poisoning-related deaths and complications,500 individuals die every year from unintentional CO poisoning, and the number of those dying from intentional CO poisoning has increased by more than 5–10 times***(Cha et al., 2013).***

Carbon monoxide (CO) is an odorless, tasteless, colorless, nonirritating gas formed by hydrocarbon combustion. The atmospheric concentration of CO is generally below 0.001 percent, but it may be higher in urban areas or enclosed environments ***(Olsen, K., 2005)***.

Carbon monoxide binds to hemoglobin with much greater affinity than oxygen (This is because carbon monoxide binds to red blood cells about

240 times more strongly than oxygen), forming carboxyhemoglobin COHb and resulting in impaired oxygen transport and utilization. Carbon monoxide may also precipitate an inflammatory cascade that results in CNS lipid peroxidation and delayed neurologic sequelae ***(Tomaszewski C, 2006)***.

AIM OF THE WORK

The aim of this work is to:

- Evaluate the demographic patterns and circumstances of CO intoxicated patients.
- Document the patterns of presentation of acute CO poisoning and evaluate the efficiency of investigations and the lines of treatment.
- To better understand the clinical significance of associated parameters on the patient outcome.
- To study the relationship between Co poisoning and oxdative stress.
- To study the outcomes and predictors of mortality in ptients with acute Co poisoning.

CARBON MONOXIDE POISONING

History:

Human beings have been poisoned by carbon monoxide gas CO since they first discovered hydrocarbon fuels. Napoleons surgeon, Larrey, noticed soldiers with CO toxicity when billeted in huts heated by wood burning stoves. Over 60 years ago american physicians were warned that chronic CO exposure could mimic many neurological conditions, such as cerebral haemorrhage, encephalitis, multiple sclerosis, spastic paraplegia, chorea and tetany ***(Walker, E., 1999)***.

The first scientific studies of the hypoxic effects of CO were described by *John Haldane (1896)*. The attachment of CO to hemoglobin, producing carboxy hemoglobin (COHb) was evaluated by ***Douglas et al. (1912)***. During the next half century, numerous studies were conducted with the principal emphasis being on high concentrations of COHb ***(Gorman et al., 2003).***

Chemistry:

CO has a molecular mass of 28.01 Daltons. It has a gas density 0.968 relative to air. CO absorption through the lungs depends on the duration of exposure, the concentration of CO in the environment and the alveolar ventilation rate. About 85% of absorbed CO combines with Hb while the

remainder attaches to myoglobin and other blood proteins ***(Baek etal., 1999)***.

CO is found naturally in the body as a byproduct of heme degradation. Heme oxygenase, found in the liver and spleen, is the major endogenous source of CO. Endogenous production of CO results in a carboxyhemoglobin (COHb) of 2% ***(Hampson etal., 2005).***

A second form of the enzyme in the brain that also produces CO behaves like nitric oxide (NO), binding to guanylate cyclase and thereby increasing cyclic guanosine monophosphate (cGMP) concentrations. Although low endogenous levels are physiologic, excessive concentrations of CO from exogenous sources may be problematic because CO persists much longer than NO. CO appears to be a neuronal messenger by virtue of the fact that as a gas it can diffuse and signal adjacent cells ***(Kao and Nanagas, 2004).***

CO is readily absorbed after inhalation. The Coburn-Forster-Kane (CFK) model allows the prediction of COHb levels based on exposure history. This model has been simplified to allow estimation of the equilibrium based on the ambient concentration of CO in ppm: COHb (%) = 100/[1 + (643/ppm CO)]. This model assumes that the individual weighs 70 kg and is not anemic. With exponential uptake, more than 4 hours may be necessary to attain equilibrium. Therefore, within minutes of high CO exposures, the arterial COHb level may actually overshoot predicted estimates prior to equilibration ***(Blumenthal ; 2001).***

Once absorbed, CO is carried in the blood, primarily bound to hemoglobin. The Haldane ratio states that CO has an approximately 200-250 times greater affinity for hemoglobin than does oxygen. Therefore, CO is primarily confined to the blood compartment, but eventually up to 15% of total CO body stores are taken up by tissue, primarily bound to myoglobin.