SOME BIOMARKERS IN CARBON MONOXIDE-INDUCED CARDIOTOXICITY

Thesis

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Abstract

Background: Carbon monoxide (CO) poisoning is a common cause of toxicological morbidity and mortality. Myocardial injury is a frequent consequence of CO poisoning. Oxidative stress affection seems to be a relevant mechanism in the pathophysiology of patients with an acute carbon monoxide (CO) poisoning.

Methodology: Cardiovascular system examination and Electrocardiography were done in fifty carbon monoxide intoxicated patients admitted to Poison Control Center, Ain Shams university Hospital. We have investigated the oxidative stress indices through the assessment of plasma level of malondialdehyde, superoxide dismutase and nitric oxide. We have also assessed the cardiac enzymes such as troponine I, beta natriuretic peptide. The carboxyhaemoglobin (COHb) levels and the relationships with electrocardiographic parameters, cardiac markers (troponin I and beta natriuretic peptide) and oxidative stress indices (superoxide dismutase, malondialdehyde and nitric oxide) were studied. Data were compared with those from 40 non-smoker healthy controls comparable in terms of age and gender.

Results : In intoxicated patients, we have found a significant increase of COHb level, malondialdehyde, nitric oxide , beta natriuretic peptide , compared to control individuals, as well as a superoxide dismutase enzyme was significantly decreased. Beta natriuretic peptide showed a positive, significant correlation with COHb level, superoxide dismutase showed a negative, significant correlation with COHb level. Electrocardiogram (ECG) changes were present in 96% of patients, whereas only 4% had a normal ECG.

Conclusions: Myocardial injury occurs frequently in patients hospitalized for CO poisoning. The oxidative stress indices are significantly affected after acute CO poisoning. We suggest that such affection could be partially mediated by CO. Patients admitted to the hospital with CO poisoning should have a baseline ECG and serial cardiac biomarkers.

Key words: (Cabon monoxide, Cardiotoxicirty, Oxidative stress).

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List of Abbreviations

ANP	Atrial natriuretic peptide
AST	Aspartate amino \transferase
ATP	Adenosine tri phosphate
BNP	Beta natriuretic peptide
CD	Conjugated diene
cGMP	Cyclic guanosine monophosphate
CK-MB	Creatin kinas-MB
CNP	C-type natriuretic peptide
CNS	Central nervous system
CO	Carbon monoxide gas
COHb	Carboxyhemoglobin
cTn	Cardiac troponin
DBP	Diastolic blood pressure
DNA	Deoxyribonucleic acid
DNS	Delayed neuropsychiatric sequelae/syndrome
ECG	Electrocardiograph
GCS	Glascow coma scale
GTP	Guanosine triphosphate
GTP	Guanosine triphosphate
HBOT	Hyperbaric Oxygen Therapy
HCO3	Bicarbonate
LDH	Lactate dehydrogenase
MBP	Myelin basic protein
MDA	Malondialdehyde
NADPH	Nicotinamide adenine dinucleotide phosphate
NO	Nitric oxide
NO_2	Nitrogen dioxide
NOS	Nitric oxide synthase
NPC-R	Natriuretic peptide clearance receptor
NT-proBNP	N-terminal proBNP peptide
O2	Oxygen
O_2^-	Superoxide radical
OH	Hydroxyl radical
$ONOO^-$	Peroxynitrite anion
PCC	Poison Control Center
PCO2	Blood partial pressure of CO2
PO2	Blood partial pressure of O2
Ppm	Parts per million

List of abbreviations cont.

PUFA	Polyunsaturated fatty acid
RBG	Random blood glucose
RNS	Reactive nitrogen species
R-O_2	Peroxy radicals
ROS	Reactive oxygen species
SBP	Systolic blood pressure
SO_2	Oxygen saturation
SOD	Superoxide dismutase
SOD-3	Extracellular superoxide dismutase

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INTRODUCTION

Carbon monoxide (CO) is a product of combustion of organic matter under conditions of restricted oxygen supply that prevents complete oxidation to carbon dioxide (CO_2). It is tasteless, odorless, non-irritating but highly toxic inhalant gases that produce fatal poisoning in many countries ***(Omaye, 2002).*** Sources of CO poisoning include any source of combustion, such as faulty furnaces, automobile exhaust, charcoal, industrial solvents, and tobacco smoke ***(Weaver, 1999).***

CO has been termed "the unnoticed poison of the 21st century". Because of its properties and because it lacks a unique clinical signature, CO poisoning is difficult to detect and can mimic other common disorders. Therefore, the true incidence of CO poisoning is unknown and many cases probably go unrecognized ***(Abelsohn et al., 2002).***

Carbon monoxide is life-threatening to humans and other aerobic forms of life, as inhaling even relatively small amounts can lead to hypoxic injury, neurological and tissue damage and, possibly death. A concentration as little as 0.04% (400 parts per million) in the air can be fatal. The gas is especially dangerous because it is not easily detected by human senses ***(Satran et al., 2006).***

Symptoms of mild poisoning include headache, vertigo and flu-like effects; larger exposures can lead to significant toxicity of the central nervous system, heart and even death. The cardiac clinical manifestations include tachycardia , hypertension, myocardial ischemia and atrial fibrillation ***(Choi, 2001).***

AIM OF THE WORK

The aim of this work is to:

- Assess the cardiotoxic effects of carbon monoxide toxicity through the estimation of cardiac biomarkers in "CO-exposed subjects".
- Investigate the possible mechanism (s) of these toxic effects by assessing the oxidative stress markers.