

**A Biochemical Study on the impact effect of
Carbon monoxide indoor intoxication
on children and adults**

By

Nageya Mohammad Amin

B. Sc.in Biochemistry Ain Shams University, 1999

Master in Environmental Science, Ain Shams University, 2002

**A Thesis Submitted in Partial Fulfillment
Of
The Requirement for the Doctor of philosophy
In
Environmental Science**

**Department of Environmental Basic Science
Institute of Environmental Studies & Research
Ain Shams University**

**A Biochemical Study on the impact effect of
Carbon monoxide indoor intoxication
on children and adults**

By

Nageya Mohammad Amin

B. Sc.in Biochemistry Ain Shams University, 1999

Master in Environmental Science, Ain Shams University, 2002

**A Thesis Submitted in Partial Fulfillment
Of
The Requirement for the Doctor of philosophy
In
Environmental Science**

**Department of Environmental Basic Science
Institute of Environmental Studies & Research**

Under The Supervision of:

Prof. Dr. Fawzia M.A. Fahim

Dead

Prof. of Biochemistry.
Faculty of Science.
Ain Shams University

Dr. Mahmoud B. Abd El-Wahab

Colleague of Biochemistry.
Poison Control Center.
Ain Shams University

**A Biochemical Study on the impact effect of
Carbon monoxide indoor intoxication
on children and adults**

By

Nageya Mohammad Amin

B. Sc.in Biochemistry Ain Shams University, ١٩٧٩

Master in Environmental Science, Ain Shams University, ٢٠٠٢

**This Thesis for the Doctor of Philosophy in Environmental
Science Has Been Approved by:**

Name	Signature
Prof. Dr. Hala Abd El Hamid Kassem	
Head of Environmental Basic science Department. Institute of Environmental Studies and Research Ain Shams University (Administrative Tight)
Prof. Dr. Mohamed M.M. Badawi	
Prof. of Biochemistry. The National Organization for Drug Control And Research (NODCAR)
Prof. Dr. Yehia Shaker M.H. Shaker
Prof. of Biochemistry. National Research Center (N.R.C)	

ENGLISH SUMMARY

Acute carbon monoxide (CO) poisoning is one of the most frequent causes of intoxication and is the most common cause of household toxic death. The accidental carbon monoxide intoxication is usually most prevalent in low economic and rural areas during winter carbon monoxide is a product of combustion of organic matter under conditions of restricted oxygen supply, which prevents complete oxidation to carbon dioxide.

Common sources of carbon monoxide that may lead to indoor intoxication include house fires, furnaces or heaters, wood – burning stoves, and propane fueled equipment such as portable camping stoves, ice resurfaces, forklifts, gasoline – powered tools such as high pressure washers, floor buffers, welders used in buildings or semienclosed spaces and cigarette smoking. Carbon monoxide is also introduced through emissions from variety of combustion sources and in the infiltration or ventilation air from outdoors.

Toxicity primarily is due to cellular hypoxia which is caused by impeded oxygen delivery. Carbon monoxide binds hemoglobin resulting in a state of relative anemia, as it binds hemoglobin 230 – 250 times more avidly than oxygen. Thus even small concentration, can result in significant levels of carboxy hemoglobin. Once the gas is inhaled, it is readily absorbed through the lungs and takes place of oxygen that is normally carried in the red blood cells. Tissues; most importantly the brain become starved for life sustaining oxygen.

Symptoms of mild poisoning include headaches, vertigo, and flu – like effects making the initial diagnosis may be difficult and are often misinterpreted, so it is known as the "silent killer". Larger



بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ

قَالُوا سُبْحَانَكَ لَا عِلْمَ
لَنَا إِلَّا مَا عَلَّمْتَنَا إِنَّكَ أَنْتَ
الْعَلِيمُ الْحَكِيمُ

صدق الله العظيم

سورة البقرة الآية ٣٢

ACKNOWLEDGEMENT

I wish to express my sincere appreciation and gratitude to **Prof. Dr. Fawzia A. Fahim**, professor of Biochemistry, faculty of science, Ain Shams University for her valuable advice, great efforts, continuous encouragement and profound reading of the manuscript.

My deep thanks are due to **Dr. Mahmoud B. Abd El-Wahab**, Colleague of Biochemistry, Poison Control Center, Ain Shams University for the suggestion of the point, his technical assistance, generous help, providing the laboratory facilities to accomplish this work, his continuous guidance, great support and efforts and his profound reading of the manuscript.

Also, I would like to express my deepest thanks and gratitude to Ass. **Prof. Dr. Wafaa Ahmad Hasan**, Head of Hormone's Evaluation Dep., National Organization for Drug Control And Research for her complete assistance in plasma neurotransmitters determination in all studied groups.

LIST OF CONTENTS

	Page
List of Tables	iii
List of Figures	iv
List of Abbreviations	v
Abstract	
I- Introduction and Aim of the work	١
I-١ Introduction	١
I-٢ Aim of the work	٣
II- Review of literature	٤
- Chemistry	٤
- Sources	٥
- Environmental levels	١٠
- Symptoms pf carbon monoxide toxication	١١
a- Acute	١١
b- Chronic	١٣
- Toxicity	١٤
- Carboxyhemoglobin	١٧
- Endogenous carbon monoxide production	٢٠
- Toxic mechanisms	٢٠
١- Hemoglobin	٢٠
٢- Myoglobin	٢٣
٣- Direct cellular toxicity	٢٥
٤- Cytochrome oxidase	٢٦
٥- Nitric oxide	٢٨
- Pregnancy	٢٩
- Elimination	٣٠
III- Experimental	٣١
III-١ Subjects	٣١
III-٢ Materials	٣١
III-٢-١ Special designed sheet	٣١
III-٢-٢ Blood gas analyzer	٣١
III-٢-٣ Plan of the work	٣١
III-٢-٤ Blood sampling and collection	٣٢
III-٢-٥ Reagents	٣٢
III-٢-٦ Instruments	٣٧
III-٣ Methods	٣٨
III-٣-١ Determination of arterial blood gases, parameters and electrolytes	٣٨
III-٣-٢ Determination of plasma glucose level	٣٨
III-٣-٣ Determination of plasma aminotransferases	٣٨

activity	
III-٣-٤ Determination of plasma urea	٣٩
III-٣-٥ Determination of plasma creatinine	٤٠
III-٣-٦ Determination of plasma creatine phosphokinase (CPK) activity	٤٠
III-٣-٧ Determination of plasma ٨ - Glutamyl transpeptidase (٨ G T) activity	٤١
III-٣-٨ Determination of plasma pseudo cholinesterase activity	٤١
III-٣-٩ Determination of plasma Insulin level	٤٢
III-٣-١٠ Determination of plasma neurotransmitters Dopamine (DA), Serotonin (٥- hydroxyl triptamine, ٥ HT) and Norepinephrine (NE)	٤٣
III-٣-١١ Statistical Analysis	٤٥
IV- Results	٤٦
V-Discussion	٦١
VI- English Summary	٩٢
VII- References	٩٥
VIII- Arabic Summary	
IX- Arabic Abstract	

LIST OF TABLES

	Page
Table (١): Changes in blood pH, PCO _r , PO _r , HCO _r ⁻ , Hb, O _r Hb and COHb in adults post CO exposure (Gr I A.P)	٤٩
Table (٢): Changes in blood Na ⁺ , K ⁺ , Cl ⁻ and A.G & plasma glucose and insulin in adults post CO exposure (Gr I A.P)	٥٠
Table (٣): Changes in plasma urea, creatinine, ALT, AST, G.G.T, P.Cholinesterase and CPK in adults post CO exposure (Gr I A.P)	٥١
Table (٤): Changes in plasma Serotonin, Dopamine and Norepinephrine in adults post CO exposure (Gr I A.P)	٥٢
Table (٥): Changes in blood pH, PCO _r , PO _r , HCO _r ⁻ , Hb, Hct, O _r Hb and COHb in children post CO exposure (Gr II Ch.P)	٥٣
Table (٦): Changes in blood Na ⁺ , K ⁺ , Cl ⁻ and A.G & plasma glucose and insulin in children post CO exposure (Gr II Ch.P)	٥٤
Table (٧): Changes in plasma urea, creatinine, AST, ALT, G.G.T, P.Cholinesterase and CPK in children post CO exposure (Gr II Ch.P)	٥٥
Table (٨): Changes in plasma Serotonin, Dopamine and Norepinephrine in children post CO exposure (Gr II Ch.P)	٥٦

LIST OF FIGURES

	Page
Fig (1): Space felling model of a carbon monoxide molecule	5
Fig (2): Oxyhemoglobin dissociation curves of normal human blood, of blood containing 5% carboxyhemoglobin and of blood with a 5% normal hemoglobin concentration due to anemia (Raub, 1999)	24
Fig (3): Pathophysiology of carbon monoxide poisoning ...	29
Fig (4): Changes in blood pH, PCO_r, PO_r and HCO_r⁻ in adults and children post CO exposure	57
Fig (5): Changes in Hb, HCT%, O_rHb% and COHb% in adults and children post CO exposure	57
Figure (6): Changes in blood Na⁺, K⁺, Cl⁻ and A.G in adults and children post CO exposure	58
Fig (7): Changes in plasma glucose and insulin in adults and children post CO exposure	58
Fig (8): Changes in plasma urea and creatinine in adults and children post CO exposure	59
Fig (9): Changes in plasma ALT, AST, GGT and CPK in adults and children post CO exposure	59
Fig (10): Changes in plasma P. cholinesterase in adults and children post CO exposure	60
Fig (11): Changes in plasma serotonin, dopamine and norepinephrine in adults and children post CO exposure	60

LIST OF ABBREVIATIONS

A.G	Anion Gap
ABGs	Arterial blood gases
ACh	Acetylcholine
ADP	Adenosine diphosphate
ALT	Alanine amino transferase
AMP	Adenosine monophosphate
AST	Aspartate amino transferase
ATP	Adenosine Triphosphate
BuCHE	Butyryl cholinesterase
CK	Creatine kinase
Cl ⁻	Chlorine ions
CNS	Central Nervous System
CO	Carbon monoxide
CO ₂	Carbon dioxide
COHb	Carboxyhemoglobin
COX	Cytochrome – C Oxidase
CPK	Creatine phospho kinase
CT	Computed Tomographic
DA	Dopamine
DOPA	Dihydroxy phenylalanine
EDTA	Ethylene diamine tetra acetic acid
Glucose 6 P.DH	Glucose 6 – Phosphate dehydrogenase
GGT	Gamma glutamyl transpeptidase
GOD	Glucose oxidase
GSH	Reduced glutathione
Hb	Hemoglobin
HCO ₃ ⁻	Carbonates
HCT	Hematocrite
HK	Hexokinase
HK	Hoxokinase
HO	Heme Oxygenase
5-HT	5-Hydroxy tryptamine
IU	International unit
K ⁺	Potassium ions
L	Liter
N	Normal
N.S	Non significant
Na ⁺	Sodium ions
NAAQS	National Ambient Air Quality Standards

NADPH	Nicotinamide Adenine Dinucleotide Phosphate
NE	Norepinephrine
NO	Nitric Oxide
O ₂ Hb	Oxyhemoglobin
OPT	Orthophaladehyde
OSSG	Oxidized glutathione
P	Plasma
PCC	Poison Control Center
PCHE	Pseudo Cholin Esterase
PCO ₂	Partial Pressure of Carbon dioxide
PCr	Phosphocreatine
PO ₂	Partial Pressure of Oxygen
Ppm	Part per million
ROS	Reactive oxygen species
S	Serotonin
SPSS	Statistical Package for social science
THB	Tetrahydro Bioprein
U	Unit
UV	Ultra violet
WHO	World Health Organization

ABSTRACT

Carbon monoxide (CO) is a significant toxic gas. It is called a “silent killer”. Acute CO poisoning is the most common type of fatal poisoning in many countries as it is one of the most frequent causes of intoxication and is the most common cause of household toxic death. This study aimed to carry out a comparative study of the effects of CO intoxication on Egyptian adults and children's, some blood gases most important biochemical & hematological parameters, enzymes, neurotransmitters and hormone insulin. This work was conducted on cases admitted to Poison Control Center (PCC) Ain Shams University Hospitals with complaint diagnosed as CO poisoning during the winter of 2006 – 2007 and then classified according to age into 2 groups: Gr I A.P (adult patients group) aging from 18 – 40 years and Gr II CH.P (Children patients group) aging from 2 - 10 years. Each group consisted of 40 patients. Control cases were also classified according to their ages into 2 groups GR III NC¹ (adult control group) and Gr IV NC² (children control group). Each group consisted of 20 normal persons.

There was a significant increase in blood pH, COHb, K⁺, plasma glucose, insulin, urea, creatinine, ALT, AST, GGT and CPK in adults and children, while a significant decrease in PCO₂, PO₂, HCO₃⁻, O₂Hb, blood Na⁺, plasma P.cholinesterase, serotonin, dopamine, and norepinephrine was recorded in both adults and children. A non significant change in hemoglobin, hematocrite and A.G was recorded in both groups. Chlorine ions were significantly decreased in children while it was insignificantly changed in adults.

Key words:

Carbon monoxide poisoning – Blood gases – indoor intoxication – Hematology – neurotransmitters – Insulin.

INTRODUCTION

Acute carbon monoxide (CO) poisoning is one of the most frequent causes of intoxication and is the most common cause of household toxic death (**Deshamps, *et al.*, ٢٠٠٣**).

Carbon monoxide poisoning occurs after the inhalation of carbon monoxide gas. Carbon monoxide is a product of combustion of organic matter under conditions of restricted oxygen supply, which prevents complete oxidation to carbon dioxide (CO₂).

Common sources of carbon monoxide poisoning include housefires, automobile exhaust, water heaters, kerosene space heaters, and furnaces. Stoves used for cooking and heating during outdoor activities also produce significant amounts of carbon monoxide, kerosene stoves also produce carbon monoxide when burned in a small tent (**Thomassen, *et al.*, ٢٠٠٤**).

Each year particularly during the heating season (winter), thousands of people are poisoned by carbon monoxide, with potentially devastating outcomes.

Carbon monoxide is a significantly toxic gas, and carbon monoxide poisoning is the most common type of fatal poisoning in many countries (**Omaye, ٢٠٠٢**). Symptoms of mild poisoning include headaches, vertigo, and flu – like effects making the initial diagnosis can be difficult and are often misinterpreted, so it is known as “silent killer” (**Krenzelok *et al.*, ١٩٩٦**). Larger exposures can lead to significant toxicity of the central nervous system, heart and even death. Once the gas is inhaled, it is readily absorbed through the lungs it binds tightly with hemoglobin and takes the place of oxygen that is normally carried in the red blood cells. Tissues; most importantly the brain; became starved for life sustaining oxygen (**Smoots & Wood, ١٩٩٨**).

Toxicity primarily is due to cellular hypoxia which is caused by impeded oxygen delivery. Carbon monoxide binds hemoglobin resulting in a state of relative anemia, as it binds hemoglobin 230 – 250 times more avidly than oxygen. Thus even small concentration, can result in significant levels of carboxy hemoglobin (COHb) (**Piantodosi, 1996; Klasner *et al.*, 1998; Olsen, 2005**). Long-term sequelae often occur. Carbon monoxide can also have severe effects on the fetus of a pregnant woman.

Hemoglobin, myoglobin and mitochondrial cytochrome oxidase are thought to be the mechanisms by which carbon monoxide produces toxic effects (**Gorman, *et al.*, 2003**).

Domestic carbon monoxide poisoning can be prevented by early detection with the use of household carbon monoxide detectors.