

Mona maghraby



# بسم الله الرحمن الرحيم

مركز الشبكات وتكنولوجيا المعلومات

قسم التوثيق الإلكتروني



Mona maghraby



# جامعة عين شمس

التوثيق الإلكتروني والميكروفيلم

## قسم

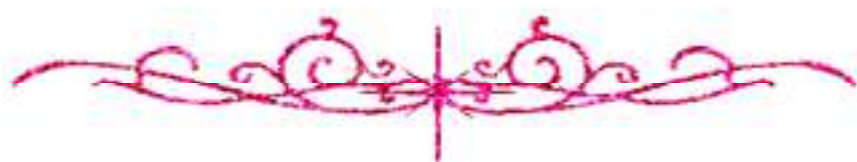
نقسم بالله العظيم أن المادة التي تم توثيقها وتسجيلها  
على هذه الأقراص المدمجة قد أعدت دون أية تغييرات



Mona maghraby



بعض الوثائق الأصلية تالفة  
وبالرسالة صفحات لم ترد بالأصل





B1A.7C

STUDY OF ATRIAL NATRIURETIC PEPTIDE LEVEL IN PATIENTS WITH  
CHRONIC OBSTRUCTIVE PULMONARY DISEASE DURING STABLE AND  
DECOMPENSATED CONDITIONS

*Thesis*

Submitted in Partial Fulfillment for the  
Master Degree of Chest Diseases and Tuberculosis

*BY*

**AHMED ABD EL-SADEK MOHAMED**

(M.B., B.Ch.)

*Supervisors*

**PROF. MEDHAT FAHMY NEGM**

Prof. and head of Department of chest diseases and tuberculosis  
Benha Faculty of Medicine

**DR. MAGDY MOHAMED OMAR**

Lecturer of Chest diseases & tuberculosis  
Benha Faculty of Medicine

**DR. MAGDY ABUL FOTOUH ABU-AMERAH**

<sup>Abu</sup>  
Lecturer of Cardiology  
Benha Faculty of Medicine

**DR. AWAD MOHAMED EL-ABD**

Lecturer of Medical Biochemistry  
Benha Faculty of Medicine

Benha Faculty of Medicine  
Zagazig University

**1999**



« بِسْمِ اللَّهِ الرَّحْمَنِ الرَّحِيمِ »

وَعَلَّمَكَ مَا لَمْ تَكُن تَعْلَمُ وَكَانَ فَضْلُ اللَّهِ  
عَلَيْكَ عَظِيمًا.

صدق الله العظيم

( النساء آية : ١١٣ )

# ACKNOWLEDGEMENT

First and foremost thanks to **ALLAH**, the most gracious and merciful.

I would like to express my sincere gratitude, deepest thanks and appreciation to Prof. **Dr. MEDHAT FAHMY NEGM**, Prof. and Head of department of chest diseases and tuberculosis, Benha Faculty of Medicine, Zagazig University, for his aware guidance, keen supervision and continuous support throughout the study without his patience and encouragement, this work would have never seen light.

I am extremely indebted to **Dr. MAGDY MOHAMED OMAR**, Lecturer of chest diseases and tuberculosis, Benha Faculty of Medicine, Zagazig University, for his generous assistance, valuable guidance.

I am so grateful to **Dr. MAGDY ABULFOTOH ABU-AMERAH**, Lecturer of cardiology, Benha Faculty of Medicine, Zagazig University, for his generous help, endless personal support and detailed supervision.

Grateful thanks to **Dr. AWAD MOHAMED EL-ABD**, lecturer of biochemistry, Benha faculty of Medicine Zagazig University. For his useful <sup>(ce)</sup> advises & kind help.

Many thanks to **Dr. AZZA AHMED IBRAHIEM**, lecturer of clinical pathology, Benha Faculty of Medicine Zagazig University. For her continuous support and kind <sup>(ce)</sup> advises.



# List of contents

<i>Title</i>	<i>page</i>
<b>Introduction</b> .....	<b>(1)</b>
<b>Aim of the work</b> .....	<b>(2)</b>
<b>Review :</b>	
* Chronic obstructive pulmonary disease .....	<b>(3).</b>
* Chronic cor- pulmonale .....	<b>(15)</b>
* Natriuretic peptides .....	<b>(21)</b>
* Biological action of atrial Natriuretic peptide .....	<b>(35)</b>
* Therapeutic trials of atrial Natriuretic peptide .....	<b>(45)</b>
* Role of atrial Natriuretic peptide in lung physiology and pathology .....	<b>(51)</b>
<b>Subjects and method</b> .....	<b>(73)</b>
<b>Results</b> .....	<b>(84)</b>
<b>Discussion</b> .....	<b>(106)</b>
<b>Summary</b> .....	<b>(117)</b>
<b>Conclusion</b> .....	<b>(119)</b>
<b>Recommendations</b> .....	<b>(120)</b>
<b>References</b> .....	<b>(121)</b>
<b>Arabic summary</b>	

# List of tables

Table no.	Title	Page no.
-----------	-------	----------

## Tables of review

I	Risk factor for COPD	7
II	Hemodynamic actions of systemic atrial natriuretic peptide ( ANP)	37
III	Central (brain ) effects of atrial natriuretic peptide ( ANP)	43

## Table of subjects and method

	Six points standard curve	80
--	---------------------------	----

## Tables of results

1	Comparison between the mean age	84
2	Sex distribution among the studied groups	84
3	Statistical Comparison of the ventilatory functions, echocardiographic data and plasma atrial natriuretic peptide ( ANP) between the control and COPD cases during exacerbation (group Ia) using unpaired t-test	85
4	Statistical Comparison of the ventilatory functions, echocardiographic data and plasma atrial natriuretic peptide ( ANP) between the control and COPD cases 6 weeks after treatment (group Ib) using unpaired t-test	86
5	Statistical Comparison of the ventilatory functions, echocardiographic data and plasma atrial natriuretic peptide ( ANP) between the control and COPD cases with cor-pulmonale and right sided heart failure (group II) using unpaired t-test	87
6	Statistical Comparison of the ventilatory functions, echocardiographic data and plasma atrial natriuretic peptide ( ANP) between the control and COPD cases without cor-pulmonale and right sided heart failure (group III) using unpaired t-test	88
7	Statistical Comparison of the ventilatory functions, echocardiographic data and plasma atrial natriuretic peptide ( ANP) between the COPD cases during exacerbation (group Ia) and 6 weeks after treatment (group Ib)) using paired t-test	89
8	Statistical Comparison of the ventilatory functions, echocardiographic data and plasma atrial natriuretic peptide ( ANP) between the COPD cases during exacerbation (group Ia) and COPD cases with cor-pulmonale and right sided heart failure (group II) using unpaired t-test	90
9	Statistical Comparison of the ventilatory functions, echocardiographic data and plasma atrial natriuretic peptide ( ANP) between the COPD cases during exacerbation (group Ia) and COPD cases without cor-pulmonale and right sided heart failure (group III) using unpaired t-test	91



10	Statistical Comparison of the ventilatory functions, echocardiographic data and plasma atrial natriuretic peptide ( ANP) between the control and COPD cases 6 weeks after treatment (group Ib) and cor-pulmonale and right sided heart failure using unpaired t-test .	92
11	Statistical Comparison of the ventilatory functions, echocardiographic data and plasma atrial natriuretic peptide ( ANP) between the control and COPD cases 6 weeks after treatment (group Ib) and COPD cases without cor-pulmonale and right sided heart failure (group III) using unpaired t-test	93
12	Statistical Comparison of the ventilatory functions, echocardiographic data and plasma atrial natriuretic peptide ( ANP) between COPD cases with (group II) and without (group III) cor-pulmonale and right sided heart failure (group III) using unpaired t-test	94
13	Correlation coefficient test between the ventilatory functions and plasma atrial natriuretic peptide ( ANP) in the different studied groups	95
14	Correlation coefficient test between echocardiographic data and plasma atrial natriuretic peptide ( ANP) in the different studied groups	96
15	Comparison between plasma ANP in the different studied groups	97

## List of figures

### Figures of review

No.	title	Page
1	Chemical structure of natriuretic peptides	22
2	Schematic diagram showing the regulation and actions of natriuretic peptides	36

### Figures of results

1	Comparison between the ventilatory functions in control group and COPD with exacerbation group (group Ia)	97
2	Comparison between the ventilatory functions in control group and COPD cases 6 weeks after treatment (group Ib)	97
3	Comparison between the ventilatory functions in control group and COPD cases with cor-pulmonale and right sided heart failure (group II)	98
4	Comparison between the ventilatory functions in control group and COPD cases without cor-pulmonale and right sided heart failure (group III)	98
5	Comparison between the ventilatory functions in(group Ia) and (group Ib)	99
6	Comparison between the ventilatory functions in(group Ia) and (group II)	99

7	Comparison between the ventilatory functions in(group Ia) and (group III)	100
8	Comparison between the ventilatory functions in(group Ib) and (group II)	100
9	Comparison between the ventilatory functions in(group Ib) and (group III)	101
10	Comparison between the ventilatory functions in(group II) and (group III)	101
11	Comparison between the mean level of ejection fraction {E.F.} % in the different studied groups	102
12	Comparison between the mean level of pulmonary artery pressure {P.A.P.} mm.Hg in the different studied groups	102
13	Comparison between the mean level of right atrial diameter ( long axis) {R.A.D. l.a. } (cm) in the different studied groups	103
14	Comparison between the mean level of right atrial diameter ( short axis) {R.A.D. s.a. } (cm) in the different studied groups	103
15	Comparison between the mean level of right diameter {R.V.D.} (cm)	104
16	Comparison between the mean level of right ventricular anterior wall thickness {R.V.A.W.T.} (cm) in the different studied groups	104
17	Comparison between the mean level of right atrial surface area {R.A.s.a.} (cm.2) in the different studied groups	105
18	Comparison between the mean plasma atrial natriuretic peptide ( ANP) level (ng/ml) in the different studied groups	105



# INTRODUCTION



## INTRODUCTION

Atrial natriuretic peptid (ANP) is a recently discovered polypeptide. Little has been written about this peptid in lung diseases, although expanded researches were done in the different cardiac conditions. It is an important hormonal regulator of salt and water and of arterial blood pressure (*Di-Nardo et al, 1992*). In the lung, it is synthesized by type II alveolar cells and respiratory epithelial cells. It is also localized in the smooth muscle cells of the pulmonary veins (not the arteries) and superior vena cava (*Springall et al., 1988*). It has been recorded in the pleural fluid in patients with congestive heart failure (*Vesely et al., 1989*).

The lung is the first and an important clearing organ for ANP (*Di-Nardo et al., 1996*). In addition to natriuresis and arterial vasodilatation including pulmonary arteries, ANP produced a C-GMP mediated broncho-relaxation and protect against histamine induced bronchoconstriction (*Kang et al., 1993*). It may prevent pulmonary edema by increasing C-GMP, decreasing intracellular  $ca^{++}$  and stabilizing tight junctions (*Di-Nardo et al., 1996*). It also stimulates surfactant production (*Ishii et al., 1989*).

These beneficial effects have led to the production of inhaled, oral and intravenous ANP to be used to modify bronchial reactivity and tone. However, as a peptid, ANP is not orally bioactive and inhalational studies for demonstrated only a mild effect (*Hulk et al., 1994*).

## **AIM OF THE WORK**

The aim of this work was to study changes of ANP in stable and decompensated cases of chronic obstructive pulmonary diseases (COPD) and to correlate these ANP changes with right atrial and right ventricular functions.

**REVIEW**



## CHRONIC OBSTRUCTIVE PULMONARY DISEASE

### DEFINITIONS

Chronic obstructive pulmonary disease (COPD) is defined as a disease state characterized by the presence of airflow obstruction due to chronic bronchitis or emphysema, the airflow obstruction is generally progressive, may be accompanied by airway hyperreactivity, and may be partially reversible (*American thoracic society, 1995*).

Chronic bronchitis is defined as the presence of chronic productive cough for 3 months in each of two successive years in a patient in whom other causes of chronic cough have been excluded (*American thoracic Society, 1995*).

Emphysema is defined as abnormal permanent enlargement of the air spaces distal to the terminal bronchioles, accompanied by destruction of their walls and without obvious fibrosis (*American thoracic Society, 1995*). Destruction is defined as lack of uniformity in the pattern of respiratory air spaces enlargement, the elderly appearance of the acinus and its components is disturbed and may be lost (*Snider et al., 1985*).

### RISK FACTORS FOR COPD

It is clear that COPD does not have a single cause, and that multiple factors must act in concert for the disorder to become clinically evident (*Baum and wolinsky, 1994*).