Study of Pulmonary Hypertension in patients with Chronic Obstructive Pulmonary Disease

Thesis
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دراسة إرتفاع ضغط الشريان الرئوى فى مرضى انسداد الشعب الهوائية المزمن

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Contents

List of Abbreviations

ALK-1 : Activin receptor-Like Kinase 1 gene.

APAH : Associated Pulmonary Arterial Hypertension.

ASE : American Society of Echocardigraphy.

BLVR : Bronchoscopic Lung Volume Reduction.

BMPR2 : Bone Morphogenic Protein Receptor 2.

CCBs : Calcium Channel Blockers.

cGMP : cyclic Glucose Mono Phosphate.

COPD : Chronic Obstructive Pulmonary Disease.

DLCO : Diffusing Lung capacity for Carbon Monoxide.

ERAs : Endothelin Receptor Antagonists.

ET-1 : Endothelin-1.

ETA : Endothelin receptor A.

ETB : Endothelin receptor B.

FPAH : Familial Pulmonary Arterial Hypertension.

FDA : Food and Drug Administration.

FEV1 : Forced Expiratory Volume in the first second.

FVC : Forced Vital Capacity.

GERD : Gastro-Esophageal Reflux Disease.

GOLD : Global initiative for chronic Obstructive Lung Disease.

5-HT : 5- Hydroxy Tryptamine (Serotonin).

5-HTT : 5- Hydroxy Tryptamine Transporter.

IPAH : Idiopathic Pulmonary Arterial Hypertension.

K : Potassium.

Kv : Voltage-dependant Potassium Channels.

NIH : National Institute of Health.

NIPPV : Non Invasive Positive Pressure Ventilation.

NIV : Non Invasive Ventilation.

NO : Nitric Oxide.

NOS : Nitric Oxide Synthase.

NYHA : New York Heart Association.

PAH : Pulmonary Arterial Hypertension.

PAP : Pulmonary Artery Pressure.

PAWP : Pulmonary Arterial Wedge Pressure.

PaCO2 : Pressure of arterial Carbon dioxide.

PaO2 : Pressure of arterial Oxygen.

PCH : Pulmonary Capillary Heamangiomatosis.

PDE-5 : 5 Phospho-Diesterase Enzymes.

PGI2 : Prostaglandin I2 (Prostacyclin).

PH : Pulmonary Hypertension.

Ppa : Pressure of pulmonary artery.

PPH : Primary Pulmonary Hypertension.

PVOD : Pulmonary Veno-Occlusive Disease.

PVR : Pulmonary Vascular Resistance.

RCTs : Respiratory Centers.

RHC : Right Heart Catheterization.

RV : Right Ventricle.

SaO2 : Saturation of Arterial Oxygen.

TNFα : Tumor Necrosis Factor Alpha.

Tx-A2 : Thromboxane- A2.

WHO : World Health Organization.

YLD : Years of Living with Disability.

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Introduction

Chronic obstructive pulmonary disease is a major health problem worldwide with increasing prevalence, morbidity, and mortality **(Nikos M. Siafakas, 2007).**

COPD is one of the leading causes of disability and death in both the developed and the developing world **(D. M. Mannino, 2007).**

According to the latest WHO estimates 2007, currently 210 million people have COPD and 3 millions died of it in 2005, and by 2030, COPD will become the 4th leading cause of death worldwide **(World Health Organization, 2007).**

COPD is defined as a disease state characterized by airflow limitation that is not fully reversible. The air flow obstruction is usually both progressive and associated with abnormal inflammatory response of the lung to noxious particles or gases**.** Cigarette smoke can induce inflammation and directly damage the lungs. It is believed that this inflammation can then lead to COPD **(Pauwels et al., 2001).**

The symptoms of COPD range from chronic cough, sputum production and wheezing to more severe symptoms, such as dyspnea, poor exercise tolerance, and signs or symptoms of right sided heart failure **(National Heart, Lung and Blood Institute, 2007).**

Pulmonary hypertension (PH) is the major cardiovascular complication of COPD and is associated with the development of corpulmonale and a poor prognosis **(Mac Nee, 1994).**

Approximately 1% of COPD patient will develop severe PH " a mean PAP > 40 mmHg", while 5% will develop moderate PH " mean PAP > 35" **(Thabut et al., 2005).**

When severe PH is diagnosed in patients with COPD, another cause of this abnormality is often present. Therefore, patients with COPD and a pulmonary mean artery pressure (Ppa) of more than 35-40mmHg or systolic pulmonary artery pressure of more than 50-55mmHg should undergo a thorough workup to look for other causes of PH **(Sajkov et al., 1999).**

Recent data suggest that there is a subgroup of patients 1 to 3% who show severe PH out of the proportion to the degree of airway impairment **(Thabut et al., 2005).**

In COPD, pulmonary vessels can undergo profound fiberocellular changes that lead to pulmonary vascular remodeling. The remodeling process is intimately related to the endothelial function. Impairment of endothelial function has been demonstrated in pulmonary arteries of patients with mild COPD **(Peinado et al., 1998).**

Considering that the endothelium plays a fundamental role in regulating the vascular tone and modulating cellular proliferation in the vessel wall, it is conceivable that changes at the endothelial level might be at the origin of the development of PH in COPD **(Dinh-Xuan et al., 1991).**

Aim of the work

The aim of the work is to study the effect of chronic obstructive pulmonary disease on pulmonary artery pressure and to identify the relation between hypoxemia and FEV1% on one hand and the degree of pulmonary hypertension on the other hand.