PERIOPERATIVE EVALUATION OF PULMONARY HYPERTENSION IN PATIENTS WITH MITRAL VALVE DISEASE

Thesis

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Abstract

Background: Left side heart disease (LHD) represents the most common causes of pulmonary hypertension (PH). Whether caused by systolic or diastolic dysfunction or valvular heart disease, the increase in left atrial pressure causes a passive increase in pulmonary pressure. In some patients, a superimposed active component caused by pulmonary arterial vasoconstriction and vascular remodeling may lead to a further increase in pulmonary arterial pressure. When present, PHTN is associated with a worse prognosis in patients with LHD. In addition to local abnormalities in nitric oxide and endothelin production, gene modifiers such as serotonin polymorphisms may be associated with the pathogenesis of PHTN in LHD.. Recent studies suggest that sildenafil, a phosphodiesterase-5 inhibitor, is a promising agent in the treatment of PHTN in LHD.

Objective: to assess the effect of the Sildenafil on the pulmonary hypertension in patient with mitral valve decease .

Patients & Methods: This study was undertaken in the Department of Cardiothoracic Surgery of Kasr El Aini Faculty of Medicine, Cairo University after approval of the local ethical committee between 2015 and 2016. It enrolled 60 adult patients submitted to mitral valve surgery having mitral valve lesion and associated with PHTN. Patients were allocated into either of 2 groups each having equal number (no=30) and properly-matched preoperative risk factors. Group A (no=30) with pulmonary artery pressure (50-80 mmHg) and group B (no=30) with pulmonary artery pressure above 80mmHg contained patients in whom Sildenafil Citrate was given . Hemodynamics (ABP, HR, CVP, PASP in mmHg) as well as mitral valve functions and LV performance (LVEF%) were assessed by clinical assessment and TEE before surgery, during ICU and hospital stay, and 6 months post –operative

Conclusion: Use of Sildenafil resulted in a significant reduction in pulmonary artery pressure

Result: . In our study in group A the mean post six month pulmonary hypertension was 28.28±5.0mmHg while in group B was 46.40± 4.8mmHg which showed an significant statistical difference as P value was 0.02.

Key word:
Mitral valve - tricuspid regurgitation –pulmonary hypertension-sildenafil

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List of Abbreviations

AF	Atrial fibrillation
CCB	Calcium Channel blocker
cAMP	Cyclic Adenine Mono Phosphate
cGMpc	Cyclic Guanine Mono Phosphate
CI	Cardiac Index
CO	Cardiac Output
COPD	Chronic Obstructive Pulmonary Disease
CPB	Cardio Pulmonary Bypass
CVP	Central Venous Pressure
DNA	Di Nucleotide Adenine
EDD	End Diastolic Dimension
EF	Ejection Fraction
EtA	Endothelin-1 receptor type A
EtB	Endothelin-1 receptor type B
FC	Function capacity
FAC	Fractional Area of Change
GTN	Glyceryl Tri-Nitrate
HPV	Hypoxic Pulmonary Vasoconstriction Reflex
ILD	Interstitial lung diseases
IPAH	Idiopathic pulmonary arterial hypertension
L	Liter
LV	Left Ventricle
LA	Left Atrium
MVP	Mitral valve prolapse
MAP	Mean Arterial Blood Pressure

Ml	Milliliter
mmHg	Millimeter Mercury
MPAP	Mean Pulmonary Artery Pressure
MR	Mitral Regurge
MS	Mitral Stenosis
NO	Nitric Oxide
OSA	Obstructive sleep apnea
NYHA	New York Heart Association
PVH	Pulmonary veins hypertension
PAOP	Pulmonary artery occlusive pressure
PDE	Phospho Di- esterase Enzyme
PVRI	Pulmonary vascular resistance index
PHTN	Pulmonary hypertension
PA	Pulmonary Artery
PAH	Pulmonary Arterial Hypertension
PAP	Pulmonary Artery Pressure
PASP	Pulmonary Artery Systolic Pressure
PCWP	Pulmonary Capillary Wedge Pressure
PDEI III	Phospho Di- esterase Enzyme Inhibitor III
PDEI V	Phospho- Di esterase Enzyme Inhibitor V
PDGF	Platlet Derived Growth Factor
PHTN	Pulmonary Hypertension
PVOD	Pulmonary Veno-Occlusive Disease
RAP	Right Atrial Pressure
RV	Right Ventricle
RVSP	Right ventricle systolic pressure

SMCS	Smooth muscle cells
SPAP	Systolic pulmonary artery pressure
SVRI	Systemic vascular resistance index
SD	Standard Deviation
SV	Stroke Volume
TTE	Trans Thoracic Echocardiography
TR	Tricuspid regurgitation
TEE	Trans esophageal Echocardiography.
6MWD	6minute walk distance

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INTRODUCTION

Left side heart disease (LHD) represents the most common causes of pulmonary hypertension (PHTN). Whether caused by systolic or diastolic dysfunction or valvular heart disease, a hallmark of PTHN associated with LHD is elevated left atrial pressure. In all cases, the increase in left atrial pressure causes a passive increase in pulmonary pressure. In some patients, a superimposed active component caused by pulmonary arterial vasoconstriction and vascular remodeling may lead to a further increase in pulmonary arterial pressure. When present, PHTN is associated with a worse prognosis in patients with LHD. In addition to local abnormalities in nitric oxide and endothelin production, gene modifiers such as serotonin polymorphisms may be associated with the pathogenesis of PHTN in LHD. Optimizing heart failure regimens and corrective valve surgery represent the cornerstone of the treatment of PHTN in LHD. Recent studies suggest that sildenafil, a phosphodiesterase-5 inhibitor, is a promising agent in the treatment of PHTN in LHD. Unloading the left ventricle with circulatory support may also reverse severe PHTN in patients with end-stage heart failure allowing candidacy to heart transplantation.

AIM OF THE WORK

This study is to be undertaken to investigate benefit of the Sildenafil in patients with pulmonary hypertension associated with mitral valve disease?

Study Design:

Prospective randomized controlled trial over sixty patients with Mitral valve disease and pulmonary hypertension undergoing corrective valve surgery.

Ethical committee approval (it was ethically approved by the department)

THE PULMONARY ARTERY

It originates from the infundibulum of the right ventricle at the pulmonary orifice. Its 5 cm in length and 3 cm wide in diameter, at about the level of fibro-cartilage between 5^{th}. & 6^{th}. thoracic vertebrae, the pulmonary trunk divides into right and left pulmonary arteries which are of nearly be equal size. The right pulmonary artery passes under the arch of the aorta more or less horizontally and before entering the hilum it divides into a superior division (which supplies the upper lobe) and the continuation of the main trunk. The left pulmonary artery takes a backward and upward course. It lies about 1cm higher than the right pulmonary artery. The remains of the ductus arteriosus of the neonate connect the left pulmonary artery to the arch of the aorta above. The artery divides into a short superior division which promptly divides into branches supplying the upper lobe. The inferior division hooks backwards over the top of the upper lobe bronchus and continues downwards and backwards lateral to and a little behind the lower lobe bronchus. In doing so it forms a vascular arch, which is seen on a lateral radiograph as a smaller curved shadow lying below that of the aorta **(Naeije, 2003)**.

Figure (1) anatomy of pulmonary artery**(Gray's Anatomy, 1985).**

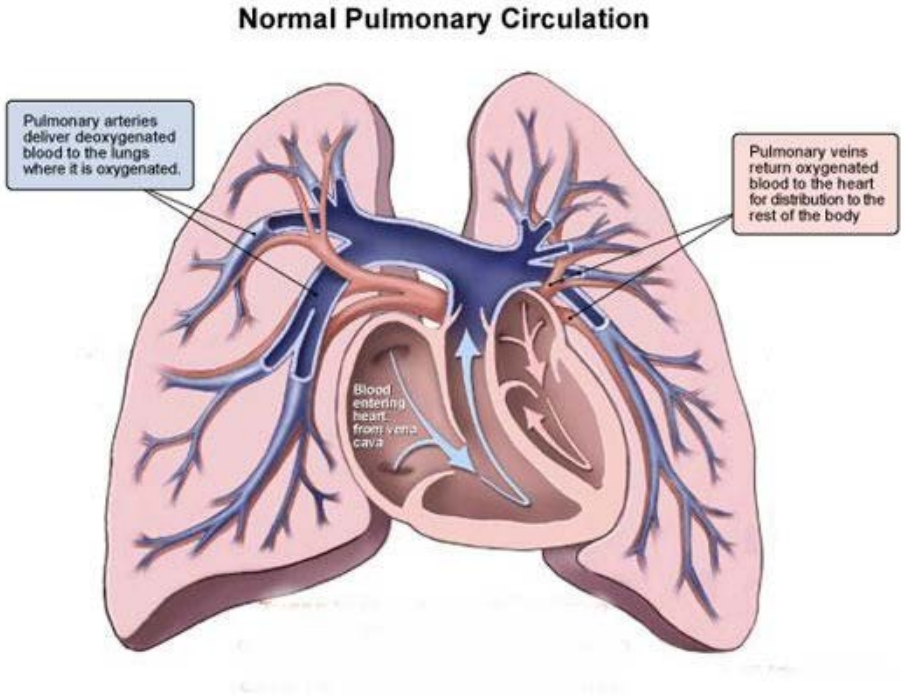

Figure (1): The Pulmonary circulation)(Gray's Anatomy, 1985)

The distribution of the pulmonary arteries within the lobes of the lungs, although broadly following the branching pattern of the bronchi, shows considerable variation. The pulmonary arterial vessels convey deoxygenated blood from RV to the lungs, consistent with the relatively thin wall of RV in comparison to that of the left ventricle; the PA vessels also have walls only 1/3 thickness of systemic vessels of comparable size **(Gray's Anatomy, 1985).**

The large pulmonary arteries have prominent concentric elastic laminae in their walls, although the walls are strikingly thinner than systemic arteries of similar diameter. Elastic arteries are found down to vessels of 1mm diameter, after which the elastic laminae become limited to internal and external laminae and between these circular

muscles are found. These small arteries are referred to as muscular arteries although the amount of muscle is slight compared with analogous systemic vessels, Vessels smaller than 100 um lose their muscular layer and have only a single elastic lamina **(Naeije, 2003)**.

Physiology of the Pulmonary Circulation

The pulmonary circulation is a high-flow and low-pressure circuit, which favors pulmonary gas exchange by preventing fluid moving out of the pulmonary vessels into the interstitial space, and allows the right ventricle to operate at a low energy cost. However because of the low pressures, the pulmonary circulation is very sensitive to mechanical influences, and the (flow generator) the right ventricle is thin walled, poorly prepared for rapid changes in loading conditions **(Poelaert & Skarvan, 2000)**.

Normal pulmonary vascular pressures and flows:

In **1970, Swan, Ganz** and their coworkers, pioneered by introducing the technology by which exploration of the pulmonary circulation can be done without fluoroscopy. It remains the gold standard for the functional evaluation of the pulmonary circulation. Progress in technology now allows refined beat-by-beat non-invasive approaches, which improves the understanding of the coupling of the right ventricle to normal and abnormal pulmonary hemodynamic conditions **(Poelaert J, Skarvan, 2000)**.