MANAGEMENT OF SECONDARY PULMONARY HYPERTENSION IN ICU

An Essay

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List of Abbreviations

ALI	Acute lung injury
ARDS	Acute respiratory distress syndrome
BPA	Balloon pulmonary angioplasty
cAMP	Cyclic adenosine monophosphate
CCB	Calcium channel blocker
cGMP	Cyclic guanosine monophosphate
COPD	Chronic obstructive pulmonary disease
CTD	Connective tissue disease
CTEPH	Chronic thromboembolic pulmonary hypertension
DLCO	Diffusing capacity of the lung for carbon monoxide;
DPAH	Drug induced PAH
ECG	Electrocardiogram
ECMO	Extracorporeal membrane oxygenation
ERA	Receptor antagonist
ET	Endothelin
ET-1	Endothelin-1
HIV	Human immune-deficiency virus
HPAH	Heritable pulmonary arterial hypertension
ICU	Intensive care unit
iNO	Inhaled Nitric oxide
IPAH	Idiopathic pulmonary arterial hypertension;
IVC	Inferior vena cava
LV	Left ventricular
LVEDP	Left ventricular enddiastolic pressure
NO	Nitric oxide
O	Oxygen

List of Abbreviations

PA	Pulmonary artery
PAH	Pulmonary arterial hypertension
PAP	Pulmonary arterial pressure
PAWP	Pulmonary artery wedge pressure
PDE5is	Phosphodiesterase type 5 inhibitors
PE	Pulmonry embolism
PEA	Pulmonary endarterectomy
PG.....	Prostaglandin
PH.....	Pulmonary hypertension
PLa	Left atrial pressure.
PVOD	Pulmonary veno occlusive disease
PVR.....	Pulmonary vascular resistance
RAP	Right atrial pressure
RCT	Randomized controlled trials
RHC	Right heart catheterization
RV	Right ventricular.
SBP	Systolic blood pressure
SMC	Smooth muscle cells
SPAH	Secondary pulmonary arterial hypertension
SSc	Systemic sclerosis
TPG	Transpulmonary pressure gradient
TRV	Tricuspid regurgitation velocity
V/Q	Ventilation/perfusion
VIP	Vasoactive intestinal peptide
VOD	Venoocclusive disease
WHOFC	World Health Organization functional class

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Abstract

Pulmonary artery pressure elevation complicates the course of many complex disorders treated in a noncardiac intensive care unit. Acute pulmonary hypertension, however, remains underdiagnosed and its treatment frequently begins only after serious complications have developed.

Pulmonary hypertension is classified according to underlying pathophysiologic mechanisms, clinical features, natural history, and response to treatment.

Therapy of acute arterial pulmonary hypertension should generally be aimed at acutely relieving right ventricular (RV) pressure overload and preventing RV dysfunction.

Cases of severe acute pulmonary hypertension complicated by RV failure and systemic arterial hypotension are real clinical challenges requiring tight hemodynamic monitoring and aggressive treatment including combinations of pulmonary vasodilators, inotropic agents and systemic arterial vasoconstrictors. The choice of vasopressor and inotropes in patients with acute pulmonary hypertension should take into consideration their effects on vascular resistance and cardiac output when used alone or in combinations with other agents, and must be individualized based on patient response.

Keywords: acute pulmonary hypertension, pulmonary hypertension, right heart failure , intensive care unit

INTRODUCTION

PH is defined as an increase in mean pulmonary arterial pressure (PAPm) ≥25 mmHg at rest as assessed by right heart catheterization (RHC) in association with variable degrees of pulmonary vascular remodelling, vasoconstriction an in situ thrombosis. ***(Hoeper et al., 2013)***

Many medical disorders managed in the intensive care unit (ICU) are associated with an elevation of pulmonary arterial pressure (PAP). Usually this is transient, of mild to moderate severity and not considered to affect patient outcome. However, serious and prolonged elevation of PAP progresses to severe acute pulmonary hypertension leading to life threatening complications including refractory systemic arterial hypotension, severe hypoxemia, right ventricular (RV) dysfunction and failure resulting in cardiogenic and/or obstructive shock and death. It is well known that left ventricular dysfunction/failure is one of the main causes of pulmonary venous hypertension, particularly in the cardiac ICU setting ***(Hoeper et al, 2002).***

Unfortunately, in most cases acute pulmonary hypertension remains under diagnosed and is usually recognized when the patient develops obvious signs of progressive RV failure. Pulmonary hypertension had been classified as being primary or secondary .

Cardiac disorders, pulmonary diseases, or both in combination are the most common causes of secondary pulmonary arterial hypertension (SPAH).

Massive PE, sepsis, and ALI are the main causes of acute arterial pulmonary hypertension in the adult patient population (***Vieillard- Baron et al, 2001***).

Pulmonary hypertension can also develop later as a result of ARDS .

Cor pulmonale is the most important consequence of pulmonary hypertension and remains a frequent cause of RV failure and death in patients with arterial pulmonary hypertension.

Preexisting pulmonary hypertension is one of the major risk factors for morbidity and mortality in cardiothoracic surgery patients (***Bernstein and Parsonnet, 2000***)and pulmonary hypertension is a major determinant of perioperative morbidity and mortality in special situations such as heart and lung transplantation, pneumonectomy, and ventricular assist device placement (***Subramaniam and Yared, 2007***).

Pulmonary artery (PA) catheterization is considered a gold standard for the diagnosis of pulmonary hypertension (***Chemla et al, 2002***).

Echocardiography has become an important tool not only for screening of chronic pulmonary hypertension, but also for diagnosing and determining the degree and clinical significance of pulmonary hypertension in critically ill patients (***Hoeper et al, 2002; Humbert et al, 2004***).

AIM OF THE WORK

To review an outline for assessment and management of secondary pulmonary hypertension in intensive care unit.

PHYSIOLOGY OF PULMONARY VASCULAR SYSTEM

Definitions

PH is defined as an increase in mean pulmonary arterial pressure (PAPm) ≥25 mmHg at rest as assessed by right heart catheterization (RHC) ***(Hoeper et al., 2013).***

Pulmonary Circulation

Pulmonary circulation is the movement of blood from the heart to the lungs for oxygenation, then back to the heart again.

Oxygen-depleted blood from the body leaves the systemic circulation when it enters the right atrium through the superior and inferior venae cavae. The blood is then pumped through the tricuspid valve into the right ventricle. From the right ventricle, blood is pumped through the pulmonary valve and into the pulmonary artery. The pulmonary artery splits into the right and left pulmonary arteries and travel to each lung. At the lungs, the blood travels through capillary beds on the alveoli where respiration occurs, removing carbon dioxide and adding oxygen to the blood. The oxygenated blood then leaves the lungs through pulmonary veins, which returns it to the left atrium, completing the pulmonary circuit. Once entering the left heart,

the blood flows through the bicuspid valve into the left ventricle. From the left ventricle, the blood is pumped through the aortic valve into the aorta to travel through systemic circulation, delivering oxygenated blood to the body before returning again to the pulmonary circulation. The pulmonary circulation, as a separate high-flow, low pressure system, is the end result of an evolutionary process aimed at the optimization of gas exchange of endothermic birds and mammals ***(West, 2013).***

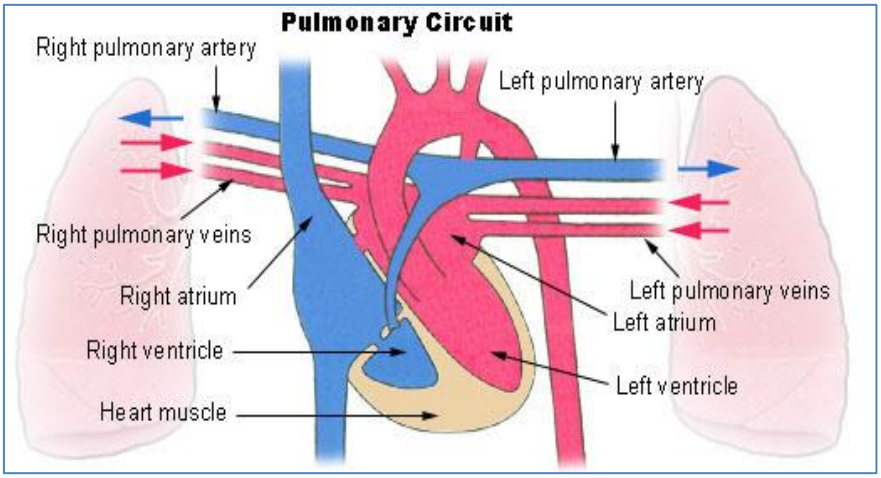

Fig. (1): Diagram of pulmonary circulation. Oxygen-rich blood is shown in red; oxygen-depleted blood in blue. Source: Boundless. "Systemic and Pulmonary Circulation." Boundless Anatomy and Physiology. Boundless, 27 Jun. 2014. Retrieved 10 Jan. 2015

(a) Pulmonary Artery Pressures and Blood Flow

The pulmonary circulation is characterized by an inflow pressure, or pulmonary artery pressure (Ppa), an outflow pressure, or left atrial pressure (Pla) and a pulmonary blood flow

(Q) approximately equal to systemic cardiac output. Pulmonary vascular pressures and flows are pulsatile. However, a simple and clinically useful description of the functional state of the pulmonary circulation may be provided by a calculation of pulmonary vascular resistance (PVR) from mean values of Ppa (mPpa), Pla and Q.

$$PVR = (mPpa - Pla) / Q$$

Measurements of pulmonary vascular pressures and cardiac output are usually performed during a catheterization of the right heart with a fluid-filled balloon-tipped thermodilution catheter ***(Swan et al., 1970).***

(b) <u>Pulmonary Capillary Pressure</u>

Wedged or occluded Ppa measurements (Ppw) are acceptable estimates of Pla, with an average gradient of 3 mmHg between the Ppw and left-ventricular end-diastolic pressure **(*Halpern and Taichman, 2009*).**

Micropuncture studies have shown that pulmonary capillary pressure (Ppc) is higher than Ppw, about halfway between arterial and venous pressures ***(Battacharya et al, 1982)***.

(c) Left Atrial Pressure and the Transpulmonary Pressure Gradient:

An increase in Pla is transmitted upstream to mPpa. The PVR equation assumes that this is in a 1/1 ratio at any given level of Q. A chronic increase in Pla may induce pulmonary vascular remodeling, and therefore lead to an "out of proportion"increase in mPpa ***(Moraes et al, 2000).*** For this reason, clinicians like to reason in terms of a transpulmonary pressure gradient (TPG) for the differential diagnosis of purely passive increase in mPpa and increased mPpa resulting from pulmonary vascular disease ***(Hoeper et al, 2009).*** The TPG is equal to the difference between mPpa and Pla.

TPG (mPpa−Pla).

The upper limit of normal of the TPG is usually assumed to be of 12mmHg ***(Hoeper et al, 2009).*** However, it is often higher than 12 mmHg in patients with left heart failure by observing an acute return of the TPG to <12 mmHg after active diuresis or after a cardiac transplantation ***(Naeije et al, 1997).***

(d) Right Ventricular Function:

The RV is functionally coupled to the pulmonary circulation ***(Champion et al, 2009).*** The structural and