Update on Anaesthetic Management of Pulmonary Arterial Hypertension in Children

Essay
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Mohamed Abd Allah Mansour

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List of Abbreviations

ACE	Angiotensinconverting enzyme
ALK1	Activin receptorlike kinase1
APAH	Associated Pulmonary Artery Hypertension
ASD	Atrial septal defect
BMPR2	Bone morphogenetic protein receptor type 2
cAMP	Cyclic adenosine monophosphate
CAV1	Caveolin1
cGMP	Cyclic guanesine monophosphate
CHD	Congenital Heart Disease
CI	Cardiac index
CO	Cardiac Output
COPD	Chronic obstructive pulmonary disease
CTD	Connective tissue disease
CTEPH	Chronic thromboembolic pulmonary hypertension
CVP	Central Venous Pressure
CXR	Chest Xray
ECG	Electrocardiogram
ECMO	Extracorporeal membrane oxygenation
EF	Ejection Fraction
EI	Eccentricity index
ENG	Endoglin
ES	Eisenmenger syndrome
ET	Endothelin
$ET_{A/B}$	Endothelin receptor subtype A/B
FPAH	Familial Pulmonary Artery Hypertension
HIV	Human immunodeficiency virus
HIV	Human immunodeficiency virus
HPV	Hypoxic Pulmonary Vasoconstriction
HR	Heart Rate
INO	Inhaled nitric oxide
IPAH	Idiopathic pulmonary arterial hypertension
IPAH	Idiopathic pulmonary arterial hypertension
Kg	Kilogram

List of Abbreviations (Cont.)

L	Liter
LA	Left Atrium
LAP	Left atrial pressure
LV	Left Ventricle
MAP	Mean Arterial Pressure
ML	Milliliter
MmHg	Millimeter Mercury
mPAP	Mean pulmonary artery pressure
6MWT	The sixminute walk test
NANC	Non adrenergic non cholinergic
NO	Nitric oxide
$PaCO_2$	Arterial carbon dioxide tension
PAH	Pulmonary arterial hypertension
PaO_2	Arterial oxygen tension
PAP	Pulmonary artrey pressure
PASP	Pulmonary Artery Systolic Pressure
PBF	Pulmonary blood flow
PCH	Pulmonary capillary hemangiomatosis
PCWP	Pulmonary Capillary Wedge Pressure
PDA	Patent ductus arteriosus
PDEI	Phospho Diesterase Enzyme Inhibitor
PFTs	Pulmonary function tests
PG	Prostaglandins
Pg	Picograms
PGI_2	Prostacyclin
PH	Pulmonary hypertension
PHVD	Pulmonary Hypertensive Vascular Disease
PI	Pulmonary insufficiency
PPH	Primary pulmonary hypertension
PPHN	Persistent pulmonary hypertension of the newborn
ppm	Parts per million
PVOD	Pulmonary VenoOcclusive Disease
PVR	Pulmonary vascular resistance

List of Abbreviations (Cont.)

PVRI	Pulmonary vascular resistance index
RAP	Right atrial pressure
REVEAL	Registry to EValuate EArly and Longterm PAH disease management
RV	Right Ventricle
RVFAC	RV fractional area change
RVSP	Right ventricular systolic pressure
SaO2	Arterial Oxygen Saturation
ScvO2	central venous saturation
sPAP	Systolic pulmonary artery pressure
SVC	Superior vena cava
SVR	Systemic vascular resistance
TAPSE	Tricuspid annular plane systolic excursion
TEE	Trans Esophageal Echocardiography
TOPP	Tracking Outcome and Practice in Pediatric Pulmonary Hypertension study
TR	Tricuspid regurgitation
TXA_2	Thromboxane A_2
VO2	Oxygen consumption
VSD	Ventricular septal defect
WHO	World Health Organisation

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Introduction

Pulmonary arterial hypertension (PAH) refers to a group of diseases that have in common narrowing of the small pulmonary arteries and arterioles resulting in progressive elevation of pulmonary vascular resistance and potential development of right ventricular failure and death (***Humbert et al., 2004).***

Pulmonary arterial hypertension is defined as a resting mean pulmonary artery pressure of more than 25 mmHg, often seen with a regurgitation velocity across the tricuspid valve of more than 2.8 m/s on Doppler echocardiography. However, this must be put into the context of the patient, especially in pediatrics where systemic mean arterial pressure may be 50 mmHg. Therefore, pulmonary hypertension is also recognized when the systolic pulmonary to systemic pressure ratio exceeds 0.5 (***Haworth and Hislop, 2009).***

Pulmonary arterial hypertension can occur idiopathically or associated with underlying conditions. The clinical classification of pulmonary hypertension (PH) categorizes PAH into idiopathic PAH, heritable PAH and PAH associated with various underlying conditions, including congenital heart defects with systemic-to-pulmonary shunt, connective tissue disease, HIV infection, portal hypertension and certain drug and toxin use (***Simonneau et al., 2009).***

Pulmonary arterial hypertension is associated with significant perioperative risk for major complications, including pulmonary hypertensive crisis and cardiac arrest. Several mechanisms of hemodynamic deterioration, including acute increases in pulmonary vascular resistance (PVR), alterations of ventricular contractility and function and coronary hypoperfusion can contribute to morbidity. Anaesthetic drugs exert a variety of effects on PVR, some of which are beneficial and some undesirable (***Robert and Glyn, 2008).***

The goals of balanced and cautious anaesthetic management are to provide adequate anaesthesia and analgesia for the surgical procedure while minimizing increases in pulmonary vascular resistance and depression of myocardial function. The development of specific pulmonary vasodilators has led to significant advances in medical therapy of PAH that can be incorporated in anaesthetic management. It is important that anaesthesiologists caring for children with PAH be aware of the increased risk, understand the pathophysiology of PAH, form an appropriate anaesthetic management plan and be prepared to treat a pulmonary hypertensive crisis (***Robert and Glyn, 2008).***

Aim of The Work

Review of up-to-date evidence regarding the anaesthetic management of pulmonary arterial hypertension in children.

Anatomy of Pulmonary Circulation

For over a thousand years, the world's view of the pulmonary circulation hewed to the teachings of Galen, who believed that blood was produced in the liver, then delivered by the right ventricle (RV) to the tissues and organs where it was consumed. In Galen's view, blood "seeped" into the left ventricle (LV) directly from the RV via invisible pores in the interventricular septum. While it may now seem self evident that this is impossible, Galen viewed blood movement as a low volume ebb and flow ***(Schultz, 2002).***

In the 13th century, Ibn al-Nafis of Syria rejected Galen's description and speculated that blood from the RV reached the LV via the lungs. While he deserves credit for the first accurate description of the pulmonary circulation, his works were lost and largely forgotten until quite recently, and it does not seem likely that they influenced the understanding of circulatory physiology in the western world ***(West, 2008).***

Fetal and Neonatal Pulmonary Circulation and Right Ventricle Development:

By the 3rd week of human gestation, passive diffusion of oxygen into the developing embryo becomes insufficient to support metabolism, blood has formed, and the primitive heart tube has begun beating; by the end of the 4th week, active circulation begins. Distinct components of the

pulmonary and systemic circulation emerge from folding and twisting of the heart tube between the 3rd and 5th weeks of gestation, under control of a complex signaling network that includes the retinoic acid and neuregulin pathways. Soon after, the RV and pulmonary circulation begin to separate from the LV and systemic circulation by formation of the interventricular septum from the endocardial cushion, and the valves develop. At birth, full septation of the interatrial septum is normally complete, with only the foramen ovale remaining as a potential shunt between the right and left atria ***(Moorman et al., 2003).***

In the embryo and fetus, the RV is the dominant chamber, accounting for about 60% of total cardiac output. Because the embryo receives oxygen and nutrients from the placenta, only 15%-25% of total cardiac output enters the lungs. The remainder of right sided cardiac output is diverted to the systemic circulation via the foramen ovale to the left atrium and via the ductus arteriosis from the pulmonary artery to the aorta. Between 40%-60%of descending aortic flow enters the placenta via the umbilical artery, then returns via the umbilical vein to the liver or through the ductus venosus to the inferior vena cava ***(Kiserud & Acharya, 2004).***

At birth, pulmonary vascular resistance falls rapidly after expansion and oxygenation of the lungs, and right ventricular cardiac output begins to flow predominantly through the pulmonary artery into the lungs. At that point,

rising left atrial pressure seals off the one way “flap valve” of the foramen ovale.At birth, RV pressures still exceed systemic pressures, but these begin to fall over the next few hours to days.Shortly thereafter, the ductus arteriosus, under control of prostaglandin, begins to close, the LV hypertrophies as it takes over the systemic circulation, and the RV atrophies.By 3 weeks of age, pulmonary pressure has normally fallen below systemic pressure, and by adulthood the normal RV is incapable of generating more than 40- 60 mmHg acutely ***(Kiserud & Acharya, 2004).***

Anatomy of the Pulmonary Circulation:

Anatomy of the pulmonary vascular trunk:

The Pulmonary artery conveys the venous blood from the right ventricle of the heart to the lung. It is a short, wide vessel, about 5 cm in length and 3 cm in diameter, arising from the conus arteriosus of the right ventricle. It extends obliquely upwards and backwards, passing at first in front and then to the left of the ascending aorta, as far as the under surface of the aortic arch, where it divides, about the level of the fibrocartilage between the fifth and sixth thoracic vertebrae into right and left branches of nearly equal size, (Figure1) ***(Paredi PBarnes, 2009).***

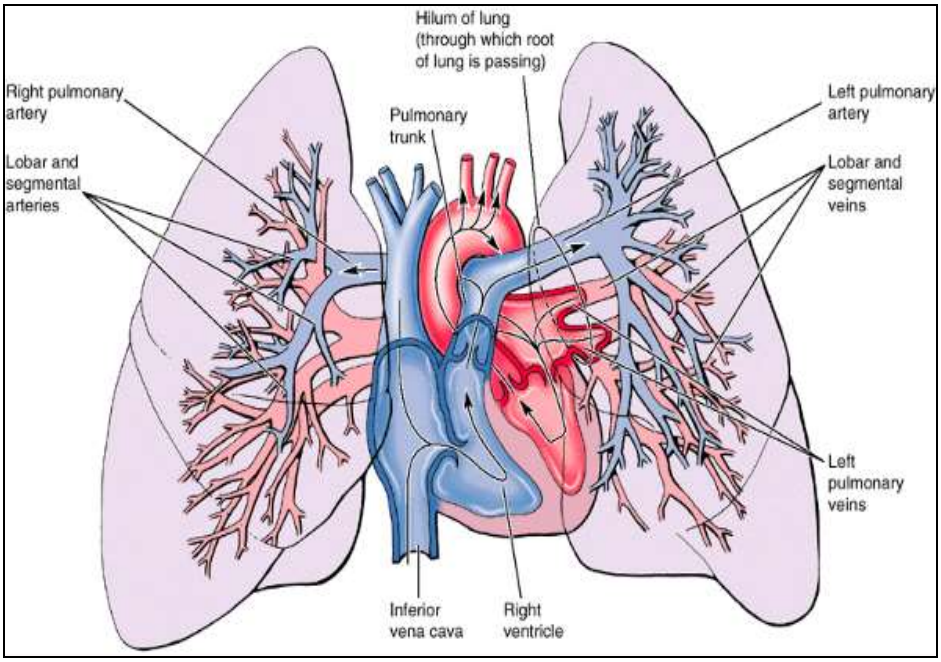

Figure (1): Pulmonary circulation ***(Moore et al., 2010).***

Relations:

The whole of this vessel is contained within the pericardium; it is enclosed with the ascending aorta in a single tube of the visceral layer of the serous pericardium, which is continued upward upon them from the base of the heart. The fibrous layer of the pericardium is gradually lost upon the external coats of the two branches of the artery. In front, the pulmonary artery is separated from the anterior end of the second left intercostal space by the pleura and left lung, in addition to the pericardium. It rests at first upon the ascending aorta, and higher up lies in front of the left atrium on a plane posterior to the ascending aorta. On either side of its origin is the auricula of the corresponding atrium or coronary artery, the left coronary artery is passing, in the first