Pulmonary Dysfunction Following Exctracorporeal Circuits

An Essay

Submitted For Partial Fulfillment of The MSc Degree
in Anesthesiology

By

Karam Ismail Ramadan Al-Khateeb
MBBCh

UNDER SUPERVISION OF

Professor Dr. Bassel Mohamed Essam Nour El-Din
Professor of Anesthesiology & Intensive Care
Faculty of Medicine
Ain Shams University

Dr. Noha Al Sayed Hussein
Lecturer of Anesthesiology & Intensive Care
Faculty of Medicine
Ain Shams University

Faculty of Medicine
Ain Shams University
2012

Acknowledgement

First and foremost I thank **ALLAH** for every thing and especially for my steady steps I have been taking in my career.

I would like to express my great appreciation and deepest gratitude to ***Prof. Dr. Bassil Mohamed Essam Nour El-Din****, Professor of Anesthesiology & Intensive Care*, Faculty of Medicine-Ain Shams University, who honored me by his kind invaluable supervision and his great support and guidance throughout the whole work.

I wish to express my deepest gratitude to ***Dr. Noha Al Sayed Hussein,*** *Lecturer of Anesthesiology & Intensive Care*, Faculty of Medicine-Ain Shams University, for her irreplaceable encouragement, her expertise and great directions all through the work.

Karam Ismail Al-Khateeb

Cairo, 2012

List of Contents

List of Abbreviations

ABG	Arterial blood gases
ALI	Acute Lung Injury
APUD	Amino Precursor, Uptake and Decarboxylation
ARDS	Acute Respiratory Distress Syndrome
BAL	Broncho-Alveolar Lavage
CABG	Coronary artery bypass grafting
C_{Dyn}	Dynamic lung compliance
cGMP	Cyclic guanosine monophosphate
CO	Cardiac output
COPD	Chronic obstructive pulmonary disease
CPAP	Continuous positive airway pressure
CPB	Cardiopulmonary bypass
CPK-MB	Creatine phosphokinase – MB portion
C_{TL}	Total lung compliance
DVT	Deep vein thrombosis
ECMO	Extracorporeal Membrane Oxygenation
F_iO2	Fraction of inspired oxygen
FRC	Functional residual capacity
HFPV	High frequency percussive ventilation
HFV	High Frequency Ventilation
I: E	Inspiration: Expiration ratio
ICU	Intensive care unit
IgE	Immunoglobulin E
IL-1	Interleukin-1
IL-2	Interleukin-2
IL-6	Interleukin-6
IL-8	Interleukin-8
IMA	Internal mammary artery
iNOS	Inducible nitric oxide synthetase
LIP	Lower inflexion point

LRM	Lung recruitment maneuver
LVP	Left ventricular pressure
Min	Minute
mmHg	Millimeter of mercury
MODS	Multiple organ dysfunction syndrome
MOF	Multiple organ failure
mRNA	Messenger RNA
NAG	N-Acetyl-D-glucosaminidase
NIV	Non invasive Ventilation
NO	Nitric oxide
NSAIDS	Non-steroidal anti-inflammatory drugs
NTG	Nitroglycerin
OLC	Open lung concept
OPCABG	Off-pump coronary artery bypass grafting
PaCO2	Arterial carbon dioxide Partial pressure
PAI-1	Plasminogen activator inhibitor-1
P_aO2	Arterial oxygen partial pressure
P_AO2	Alveolar oxygen partial pressure
PCV	Pressure-controlled ventilation
PD	Pulmonary disease
PEEP	Positive end expiratory pressure
PFC	Perfluorochemical
PLV	Partial Liquid Ventilation
PLVS	Protective Lung Ventilation Strategies
PMNs	Polymorphonuclear cells
PMX	Polymyxin
ppm	Parts per million
P-V curve	Pressure-volume curve
R_{aw}	Airway resistance
SIRS	Systemic inflammatory response syndrome
SNP	Sodium Nitroprusside
TGI	Tracheal Gas Insufflation
TLC	Total lung capacity
TNF-α	Tumor necrosis factor – alpha
TNF- β	Tumor necrosis factor – beta
T_V	Tidal volume

UIP	Upper inflexion point
VALI	Ventilator-Associated Lung Injury
VC	Vital capacity
VILI	Ventilator- Induced Lung Injury

List of Figures

List of Tables

INTRODUCTION

The primary function of the respiratory system is to exchange oxygen and carbon dioxide between the body and the environment.

Postoperative respiratory dysfunction is a well recognized side effect of cardiac operations. About 25% of patients who do not present any severe cardiac dysfunction following open heart surgery are reported to have a significant respiratory impairment for eat least one week after operation ***(Rubens and Mesana, 2004)***.

Pulmonary injury after cardiopulmonary bypass (CPB) is a common complication in patients undergoing cardiac surgery and is associated with low arterial oxygen tension (PaO_2) or high carbon dioxide tension (PCO_2), which can continue for several days, leading to prolonged mechanical ventilation. Inflammatory response to CPB ***(Nakanishi et al., 2006)*** and ischemic damage of the lungs have been considered as major causes of respiratory failure after cardiac surgery, and there have been numerous reports of successful reduction of post-CPB lung injury by controlling inflammatory response or pulmonary ischemia. Nevertheless, few of these treatments or strategies have been applied in clinical practice ***(Shoji et al., 2005)***.

The incidence of ALI in patients undergoing anesthesia with preoperative P/F ratios < 300 is approximately 20%. These patients are managed in a similar format that does not use LPVS regardless of the

etiology of their hypoxia, and the Vt settings appear to mirror the ventilator settings provided to patients in the ICU. Overall, it appears risk factors for mortality at 90 days include increased PIP and preexisting ALI. Further study is required to determine if the use of LPVS intraoperatively has a substantive impact in reducing mortality of hypoxic patients who undergo surgery both with and without ALI ***(Blum, 2011).***

Intensive care unit (ICU) ventilator management of patients with ALI involves minimizing ventilator associated lung injury by using lower tidal volumes (VT) of 6 ml/kg predicted body weight (PBW) and limiting plateau pressures to less than 30 cm H2O combined with moderate positive end-expiratory pressure (PEEP) in a lung protective ventilation strategy (LPVS) ***(Dos Santos, 2008).***

In addition, aggressive PEEP and recruitment maneuvers have been successfully used to improve oxygenation while reducing potential oxygen toxicity and alveolar shear stress, although they have not been found to provide mortality benefit ***(Mercat, 2008).***

Reinstitution of tracheal intubation and mechanical ventilation increases the use of intensive care unit and hospital resources and severely affects morbidity and mortality ***(Hein et al., 2006)***.

Noninvasive positive pressure ventilation (NPPV) has become a standard of care in acute respiratory failure ***(Hess et al., 2004).*** However, little and controversial data are available on its usefulness in

post-extubation failure after major surgery and in particular after cardiac procedures ***(Keenan et al., 2004)***.

A large number of pharmacologic therapies have been evaluated in clinical trials for the treatment of ALI/ARDS. These treatments include glucocorticoids, surfactants, inhaled nitric oxide, antioxidants, protease inhibitors, and a variety of other anti-inflammatory treatments. Unfortunately, to date none of these pharmacologic treatments has proven to be effective ***(Cepkova & Matthay, 2006)***, although some of them may be effective in a subgroup of patients with specific causes of lung injury that might make them more responsive than others. However, despite the lack of a specific pharmacologic treatment, lung-protective ventilation has reduced the mortality of ALI from 40% in 2000 to 25% in 2006 ***(Wheeler et al., 2006)***.

One of the most promising fields of research in acute lung injury is the use of adult mesenchymal stem cells (MSC) in the treatment of ALI and ARDS. Preclinical studies suggest that MSC may have a role in the treatment of ALI. Although the experimental data suggest a potential benefit of MSC cell-based therapy for ALI, further studies are needed to evaluate the mechanisms and pathways of benefit and to test both safety and efficacy ***(Lee et al., 2009)***.

RESPIRATORY PHYSIOLOGY

The primary function of the respiratory system is to exchange oxygen and carbon dioxide between the body and the environment.

Respiration as a term generally used includes two processes:

1- **External Respiration**: It is concerned with the exchange of gas between the environment and the lungs, the transfer of gases across the respiratory membranes and the transport of gases by the blood to and from the body cells.

2- **Internal respiration:** It is concerned with the oxygen consumption by the body cells through metabolic transformation ***(Boyle, 1997)***.

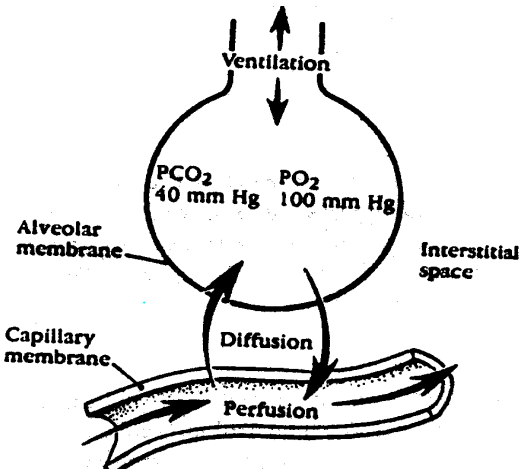

Figure-1: Diagrammatic representation of the process of ventilation, diffusion and perfusion in the lung (Guyton, 2006).

Functional Respiratory Anatomy

The structure of the chest wall

The lungs are not capable of inflating themselves; inflation is achieved by changing the dimensions of the chest wall by means of the respiratory muscles. The principal respiratory muscles are the diaphragm and the internal and external intercostal muscles. The external intercostal muscles are arranged in such a way that they lift the ribs upwards and outwards as they contract. The internal intercostal muscles pull the ribs downwards, in opposition to the external intercostal muscles. In addition, some other muscles, which are not involved during normal quiet breathing, may be called upon during exercise. These are the accessory muscles, which assist inspiration and the abdominal muscles, which assist expiration ***(Guyton, 2006)***.

The chest wall is lined by a membrane called the parietal pleura. This is separated from the visceral pleura (which cover the lungs) by a thin layer of liquid which serves to lubricate the surfaces of the pleural membranes as they move during respiration. The total volume of intrapleural fluid is about 10 ml. It is an ultrafiltrate of plasma and is normally drained by the lymphatic system that lies beneath the visceral pleura. The pleural membranes themselves are joined at the roots of the lungs. They consist of two layers of collagenous and elastic connective tissue. Beneath the visceral pleura lies the limiting membrane of the lung itself which, together with the visceral pleura, limits the expansion of

the lungs. The lungs are separated from the chest wall only by the pleural membranes ***(Guyton, 2006).***

The Structure of the airway

The trachea and the primary bronchi are held open by C-shaped rings of cartilage. In the smaller bronchi, this role is taken by overlapping plates of cartilage. The bronchioles, which are less than 1 mm diameter, have no cartilage. The absence of cartilage from the bronchioles allows them to be easily collapsed when the pressure outside the lung exceeds the pressure in the airways; this happens during a forced expiration ***(Guyton, 2006).***

Humidification and filtering of inspired air are functions of the upper airway (nose, mouth, and pharynx). The function of the tracheobronchial tree is to conduct gas flow to and from the alveoli. Dichotomous division (each branch dividing into two smaller branches), starting with the trachea and ending in alveolar sacs, is estimated to involve 23 divisions, or generations. With each generation, the number of airways is approximately doubled. Each alveolar sac contains, on average, 17 alveoli. An estimated 300 million alveoli provide an enormous membrane (50–100 m^2) for gas exchange in the average adult ***(Morgan et al., 2005)***.

Alveoli

Alveolar size is a function of both gravity and lung volume. The average diameter of an alveolus is thought to be 0.05–0.33 mm. In the upright position, the largest alveoli are at the pulmonary apex, whereas the smallest tend to be at the base. With inspiration, discrepancies in alveolar size diminish ***(Morgan et al., 2005***).

Each alveolus is in close contact with a network of pulmonary capillaries. The walls of each alveolus are asymmetrically arranged. On the thin side, where gas exchange occurs, the alveolar epithelium and capillary endothelium are separated only by their respective cellular and basement membranes; on the thick side, where fluid and solute exchange occurs, the pulmonary interstitial space separates alveolar epithelium from capillary endothelium. The pulmonary interstitial space contains mainly elastin, collagen, and perhaps nerve fibers. Gas exchange occurs primarily on the thin side of the alveolocapillary membrane, which is less than 0.4 m thick. The thick side (1–2 m) provides structural support for the alveolus ***(Morgan et al., 2005).***

The pulmonary epithelium contains at least two cell types. Type I pneumocytes are flat and form tight (1-nm) junctions with one another. These tight junctions are important in preventing the passage of large oncotically active molecules such as albumin into the alveolus. Type II pneumocytes, which are more numerous than type I pneumocytes (but because of their shape occupy less than 10% of the alveolar space),