New Treatment Modalities of Acute Lung Injury

Essay

Submitted for Partial Fulfillment
of Master Degree
in Intensive Care Medicine

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2012

جامعة عين شمس
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الطرق الحديثة في علاج مرض الإصابة الرئوية الحادة

رسالة مقدمة من

الطبيب/ محمد مجدى محمد شلبي
بكالوريوس الطب والجراحة
كلية الطب
جامعة الزقازيق

توطئة للحصول علي درجة الماجستير
في الرعاية المركزة

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2012

ACKNOWLEDGMENT

First of all I would like to thank ALLAH for all the power and support he gave me to finish this work.

I would like to express my deepest thanks, gratitude and respectful appreciation to ***Prof. Dr. Azza Abd El-Rashid Hassan,*** *Prof. of anesthesia, Faculty of medicine, Ein-Shams University, to whom I'm deeply grateful for her constant supervision and encouragement without which I would not have been able to complete this work.*

Also, I would like to express my sincere thanks to ***Dr. Rasha Gamal Abo-Sinna.*** *Lecturer of anesthesia, Faculty of medicine, Ein-Shams University, to whom I'm greatly indebted for her continuous interest and honest advices during the preparation and finalization of this work.*

I would like to express my deep thanks to all staff members of anesthesia department, and my family for their support and help.

List of abbreviations

ACE_2 : Angiotensin-Converting Enzyme-2

AECC: American European Consensus Conference

ALI: Acute Lung Injury

APACHE: Acute Physiology And Chronic Health Evaluation

APRV: Airway Pressure Release Ventilation

ARDS: Acute Respiratory Distress Syndrome

BALF: Broncho Alveolar Lavage Fluid

BMPC: Bone Marrow Progenitor Cell

C_T: Total Compliance of the respiratory apparatus

C_L: Compliance of the Lungs

C_W: Compliance of the chest Wall

CMV: Controlled Mechanical Ventilation

CT: Computed Tomography

DAD: Diffuse Alveolar Damage

DIC: Disseminated Intravascular Coagulopathy

DVT: Deep Venous Thrombosis

$ECCO_2R$: Extracorporeal Carbon Dioxide Removal

ECMO: Extracorporeal Membrane Oxygenation

ERV: Expiratory Reserve Volume

EIT: Electrical Impedance Tomography

eNOS: Endothelial Nitric Oxide Synthase

ESs: Embryonic Stem Cells

ETI: Endo-Tracheal Intubation

EVD: Extravascular Lung Density

EVLW: Extra Vascular Lung Water

FRC: Functional Residual Capacity

FVC: Forced Vital Capacity

FiO_2: Inspiratory Fraction of Oxygen

GST: Glutathione-S-Transferase

HFV: High-Frequency Ventilation

HFJV: High-Frequency Jet Ventilation

HFOV: High-Frequency Oscillatory Ventilation

HSCSs: Hematopoietic Stem Cells

IC: Inspiratory Capacity

ICU: Intensive Care Unit

IKB: Inhibitory Kappa B

IL: Interleukin

IMV: Intermittent Mandatory Ventilation

IRV: Inspiratory Reserve Volume

IRV: Inverse Ratio Ventilation

KGF: Keratinocyte Growth Factor

LIS: Lung Injury Score

MMPs: Matrix Metalloproteases

MMV: Mandatory Minute Ventilation

MODS: Multi organ Dysfunction Syndrome

MSCs: Mesenchymal Stem Cells

NAC: N-acetylcycteine

NIPPV: Noninvasive Positive-Pressure Ventilation

NFKB: Nuclear Factor kappa B

NO: Nitric Oxide

PAOP: Pulmonary Artery Occlusion Pressure

P_AO_2 : Alveolar O_2 Tension

PaO_2 : Arterial O_2 Partial Pressure

PCV: Pressure Control Ventilation

PDGF: Platelet-Derived Growth Factor

PE: Pulmonary Embolism

PEEP: Positive End Expiratory Pressure

PET: Positron Emission Tomography

PFCs: Perfluorocarbons

PLV: Partial Liquid Ventilation

PN: Parenteral Nutrition

PTCER: Pulmonary Transcapillary Escape Rate

PVR: Pulmonary Vascular Resistance

Qva: Venous Admixture

RAGE: Receptor for Advanced Glycated End Products

RM: Recruitment Maneuver

ROS: Reactive Oxygen Species

RV: Residual Volume

SARS: Severe Acute Respiratory Syndrome

SIMV: Synchronized Intermittent Mandatory Ventilation

SIRS: Systemic Inflammatory Response Syndrome

SLB: Surgical Lung Biopsy

SP: Surfactant Proteins

TEE: Trans Esophageal Echocardiography

TGF-β: Transforming Growth Factor beta

TIMPs: Tissue Inhibitors of Metalloproteases

TLB: Transbronchial Lung Biopsy

TLC: Total Lung Capacity

TNF: Tumor Necrosis Factor

TPP: Transpulmonary Pressure

TRALI: Transfusion Related Acute Lung Injury

VC: Vital Capacity

V/Q: Ventilation-Perfusion Ratio

Vt: Tidal Volume

VWF: Von-Willebrand Factor antigen

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Introduction

Acute lung injury (ALI) is defined as an acute lung disease with bilateral pulmonary infiltrates in chest radiography consistent with the presence of edema, absence of clinical evidence of left atrial hypertension, and a pulmonary wedge pressure of 18 mmHg or less. Additionally, the ratio of arterial oxygen tension to the fraction of inspired oxygen (PaO_2/FiO_2) must be 300 mmHg or less. Acute respiratory distress syndrome (ARDS), the most severe form of ALI, is defined by a ratio of arterial oxygen tension to fraction of inspired oxygen of 200 mmHg or less **(Rocco and Pelosi, 2008).**

Acute lung injury is caused mainly by either **direct lung injury** (due to aspiration pneumonia, pneumonia, fat emboli, inhalation injury, near drowning , and reperfusion injury) or **indirect lung injury** (due to transfusion related acute lung injury (TRALI), sepsis, acute pancreatitis, burns, drug overdose, head injury, and trauma) **(Ware and Matthay, 2000).**

Despite much improvement in the understanding of ALI pathophysiology and recent success in therapy, the mortality rate remains high at 35-40%. The incidence of mortality in trauma patients is relatively low (10-15%); the highest number of deaths was observed in patients with sepsis, pneumonia, or aspiration **(Phua et al., 2009).**

The course of ALI can be described in three overlapping phases. The acute or exudative phase starts from the 2nd day and lasts for up to 7 days from onset and is characterized by the development of hypoxemia, infiltrates on the chest radiograph, and a reduction in pulmonary compliance. These clinical changes are accompanied by leakage of protein-rich fluid in the alveoli, hemorrhage, and diffuse neutrophilic

alveolar infiltrates with resultant endothelial and epithelial injury **(Brun-Buisson et al., 2004).**

The sub-acute or proliferative phase of ALI occurs from day 5 onwards. It is characterized by persistent hypoxemia, increased dead space, and reduced lung compliance. This is accompanied by interstitial fibrosis, and disruption of capillary function. In some patients, these changes resolve and clinical improvement follows whereas other patients progress into the chronic or fibrotic stage. This stage results from widespread pulmonary fibrosis and loss of the normal lung structure leading to worsening lung compliance and an increase in dead space. This chronic stage usually starts as early as 14 days and lasts for many weeks **(McCallum and Evans, 2005).**

The goal of treatment for ALI/ARDS is to prevent further lung injury, reduce lung edema, and maintain tissue oxygenation. Treatment may be non-pharmacologic or pharmacologic. The non-pharmacological treatment includes: mechanical ventilation with lung protective strategy and fluid management strategies. The pharmacological treatment includes: anti-inflammatory therapy, beta-adrenergic agonists, anticoagulants, vasodilators: either non-selective (nitoprusside, hydralazine) or selective (prostaglandin E_1, prostacyclin), corticosteroids, phosphatidic acid inhibitors, and anti-oxidants **(Briel et al., 2010).**

New modalities in treatment of ALI include: extracorporeal membrane oxygenation, surfactant, inhaled nitric oxide, pentoxifylline and lisofylline, hydroxymethylglutaryl-coenzyme A reductase inhibitors, activated protein C, endothelin receptor antagonists, prostaglandin I_2, antibody to tumor necrosis factor (TNF), recombinant interleukin (IL)-1 receptor antagonists, anticytokine therapy, and cell based therapy**(Craig et al., 2011).**

Aim of the Essay

The aim of the present study is to focus on the recent treatment modalities of acute lung injury.

Anatomy of the lung

The lung is the essential organ of respiration in all air-breathing animals. To completely explain the anatomy of the lungs, it is necessary to discuss the passage of air through the mouth to the alveoli. Once air progresses through the mouth or nose, it travels through the oropharynx, nasopharynx, the larynx, the trachea, and a progressively subdividing system of bronchi and bronchioles until it finally reaches the alveoli where the gas exchange of carbon dioxide and oxygen takes place **(Wienberger et al., 2000)**.

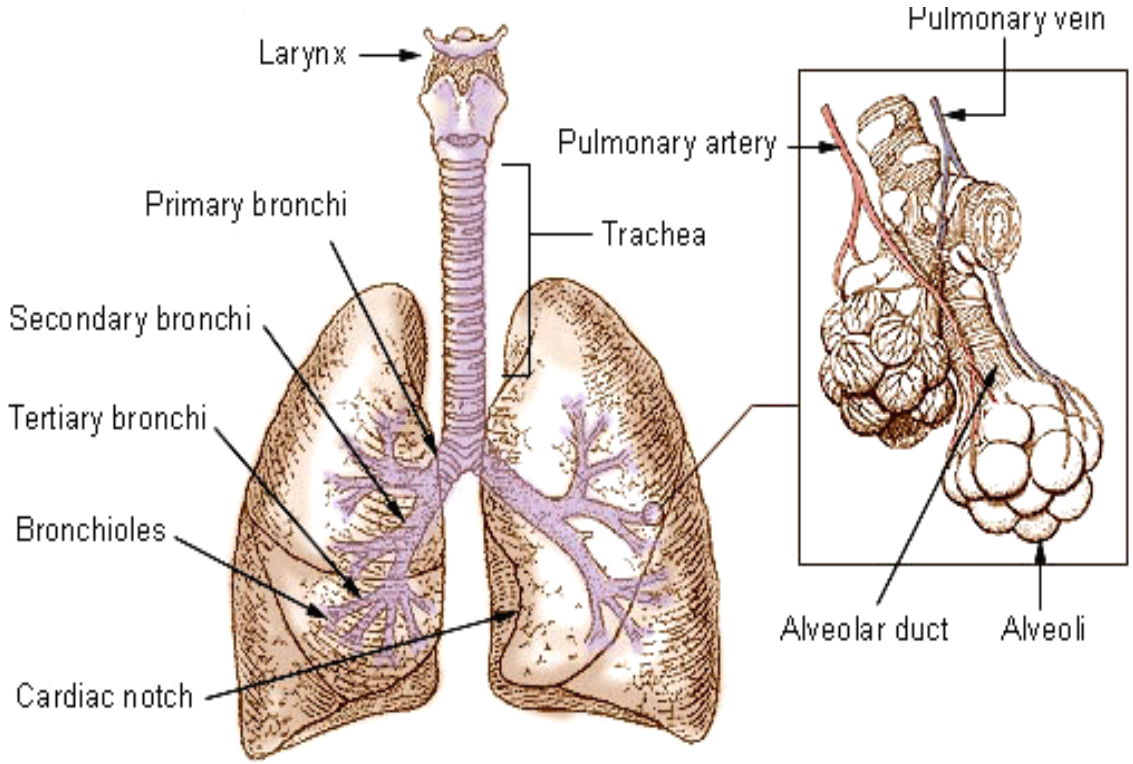

Figure (1): Bronchi, bronchial tree, and lungs **(Rogan et al., 2004)**

Humans have two lungs, with the left being divided into two lobes and the right into three lobes. Together, the lungs contain approximately 2400 km of airways and 300 to 500 million alveoli, having a total surface area of about 70 m^2 in adults. Each lung weighs 1.1 kilogram, therefore making the entire organ about 2.3 kilogram. The conducting zone contains the trachea, the bronchi, the bronchioles, and the terminal bronchioles. The respiratory zone contains the respiratory bronchioles, the alveolar ducts, and the alveoli. The conducting zone has no gas exchange with the blood, and is reinforced with cartilage in order to hold open the airways. The conducting zone warms the air to 37 degrees Celsius and humidifies the air. It also cleanses the air by removing particles via cilia located on the walls of all the passageways. The respiratory zone is the site of gas exchange with blood **(Walter, 2004)**.

Anatomy of airways:

The larynx lies at the level of upper cervical vertebrae, C4-6, and its main structural components are the thyroid and cricoid cartilages, along with the smaller arytenoid cartilages and the epiglottis, which sit over the laryngeal inlet. A series of ligaments and muscles link these structures, which, by a co-ordinated sequence of actions, protect the larynx from solid or liquid material during swallowing as well as regulating vocal cord tension for phonation. The technique of cricoid pressure is based on the fact that the cricoid cartilage is a complete ring, which is used to compress the esophagus behind it against the vertebral bodies of C5-6 to prevent regurgitation of gastric contents into the pharynx. The thyroid and cricoid cartilages are linked anteriorly by the cricothyroid membrane, through which access to the airway can be gained in an emergency **(Albertine et al., 2005)**.