Role of Low Tidal Volume, High Positive End-Expiratory Pressure Ventilation in Acute Respiratory Distress Syndrome

An Essay

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دور التنفس الصناعي باستخدام حجم مدي صغير وضغط إيجابي مرتفع بنهاية الزفير في متلازمة الضائقة التنفسية الحادة

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List of Abbreviations

ACE	**Angiotensin-converting enzyme.**
ADH	**Antidiuretic hormone.**
ANP	**Atrial natriuretic peptide.**
APC	**Activated protein C.**
AECC	**American European Consensus Conference.**
ALI	**Acute lung injury.**
ARDS	**Acute respiratory distress syndrome.**
BAL	**Bronchoalveolar lavage .**
BALF	**Bronchoalveolar lavage fluid.**
BAMPS	**Bilateral anterior magnetic phrenic nerve stimulation**.
b- FGF	**Basic fibroblast growth factor.**
BMPC	**Bone marrow progenitor cell.**
BOOP	**Bronchiolitis obliterans organizing pneumonia.**
CMV	**Controlled mechanical ventilation.**
CO	**Cardiac output.**
CPAP	**Continous positive airway pressure.**
DAD	**Diffuse alveolar damage.**
DIC	**Disseminated intravascular coagulation.**
DO_2	**Oxygen delivery.**
DVT	**Deep venous thrombosis.**
ECCOiR	**Extracorporeal carbon dioxide removal**
ECLA	**Extracorporeal lung assist.**
ECMO	**Extracorporeal membrane oxygenation.**
ECP	**Eosinophil cationic protein.**
EGF	**Epidermal growth factor.**
ES cells	**Embryonic stem cells.**
FiO_2	**Fraction of inspired oxygen.**
FRC	**Functional residual capacity.**

GIT	**Gastrointestinal.**
GFR	**glomerular filtration rate.**
Hb	**Hemoglobin concentration.**
HFV	**High frequency ventilation.**
HFJV	**High frequency jet ventilation.**
HFOV	**High frequency oscillatory ventilation.**
HPV	**Hypoxic pulmonary vasoconstriction.**
HSC	**Hematopoietic stem cell.**
IC AM	**Intercellular adhesion molecule.**
ICU	**Intensive care unit.**
ILGF	**Insulin like growth factor.**
IL	**Interleukin.**
LEFPV	**Low-frequency positive- pressure ventilation**
LIP	**Lower inflection point.**
LIS	**Lung injury score.**
MCP	**Monocyte chemoattractant protein.**
MMP	**Matrix metalloproteases.**
MODS	**Multiple organ dysfunction syndromes.**
MV	**Mechanical ventilation.**
NHLI	**National Heart and Lung Institute.**
NIPPV	**Non invasive positive pressure ventilation.**
NO	**Nitric oxide .**
NOS	**Nitric oxide synthase.**
$PaCO_2$	**Arterial carbon dioxide tension.**
PaO_2	**arterial oxygen tension**
PAOP	**Pulmonary artery occlusion pressure.**
PCWP	**Pulmonary capillary wedge pressure.**
PDGF	**Platelet derived growth factor.**
PE	**Pulmonary embolism.**
PEEP	**Positive end expiratory pressure.**

PEEPi	**Intrinsic Positive end expiratory pressure.**
PFCs	**Perfluorocarbons.**
PLV	**Partial liquid ventilation.**
PP	**Pulse pressure.**
PPM	**Parts per million.**
PPmax	**Maximum pulse pressure.**
PPV	**Positive-pressure mechanical ventilation.**
PV Curve	**Pressure-Volume curve.**
PVR	**Pulmonary vascular resistance.**
$PvCO_2$	**Venous carbon dioxide tension.**
ROS	**Reactive oxygen species.**
RAS	**Rennin angiotensin system.**
RNS	**Reactive nitrogen species.**
SaO_2	**Arterial oxygen saturation.**
SARS	**Sever acute respiratory distress.**
SIRS	**Systemic inflammatory response syndrome**
SP	**Surfactant proteins.**
SPmax	**Maximum systolic pressure.**
SV	**Stroke volume.**
SvO_2	**Mixed venous oxygen saturation.**
TLB	**Transbronchial lung biopsy.**
TGF	**Transforming growth factor.**
TA_2	**Thromboxan A_2.**
TNF	**Tumour necrosis factor.**
TRALI	**Transfusion-related acute lung injury.**
UIP	**Upper inflection point.**
VALI	**Ventilator associated lung injury.**
VEGF	**Vascular endothelial growth factor.**
VCAM	**Vascular cell adhesion molecule.**
VD	**Dead space.**

VIDD	**Ventilator-induced diaphragmatic dysfunction**.
VILI	**Ventilator induced lung injury.**
VT	**Tidal volume.**
V/Q	**Ventilation- perfusion.**

Summary

Acute respiratory distress syndrome (ARDS) is an acute inflammatory reaction of the lung with damage to the epithelial-endothelial barrier, causing high permeability pulmonary edema. It is characterized by a acute onset of severe hypoxemia, bilateral pulmonary infiltrates and a normal pulmonary artery occlusive pressure. It usually develops over 4–48 hours and persists for days or weeks. Different intra-pulmonary etiologies, such as pneumonia and aspiration and extra-pulmonary etiologies, such as septicaemia, burns, acute pancreatitis and massive blood transfusion may trigger this process.

ARDS affects approximately 200,000 patients annually in the U.S. and accounts for 10-15% of intensive care unit admissions. Between a third and a half of people with ARDS die, but mortality depends on the underlying cause.

Mechanical ventilation (MV) is an often life-saving treatment, but, as with any therapy, mechanical ventilation may expose patients to many side effects. Ventilator-induced lung injury can be defined as acute lung injury directly induced by mechanical ventilation. Also MV can cause activation of inflammatory cells and the release of inflammatory mediators that pass from the lung to the systemic circulation. So, mechanical ventilation is often a persistent “aggravating” factor in the critically ill patient “hitting” the 70 m^2 surface area of the lung 10 or more times a minute. Thus MV may lead to the development of multiple organ dysfunction syndrome.

There is no specific treatment for ARDS, measures to protect against complications and supportive care management remain the only available treatment, and since hypoxemia is the hallmark of the disease, thus

Introduction

Mechanical ventilation is one of the therapeutic cornerstones of critical care medicine. Indeed, it was mechanical ventilation therapy that really led to the creation of intensive care units (ICUs) and the development of critical care as a specialty ***(Ewan and Niall, 2009).***

The primary goal of ventilatory support is the maintenance of adequate, but not necessarily normal, gas exchange, which must be achieved with minimal lung injury and the lowest possible degree of hemodynamic impairment, while avoiding injury to distant organs such as the brain ***(Shin, 2007).***

Acute lung injury (ALI) and acute respiratory distress syndrome (ARDS) are common problems in the ICU and can complicate a wide spectrum of critical illness. ALI and ARDS are caused by an insult to endothelial and epithelial cells in the lungs assosiated with neutrophilic alveolitis, release of mediators, and increased vascular and alveolar permeability with interstitial and/or alveolar edema formation resulting in alveolar collapse and thereby arterial hypoxemia ***(Bernard et al., 1999).***

Mechanical ventilation commonly used to improve gas exchange in these patients may itself contribute to lung injury including pneumothorax, alveolar edema, and alveolar rupture. Also, mechanical ventilation using high tidal volumes and low levels of positive end-expiratory pressure (PEEP) can aggravate preexisting lung inflammation, resulting in increased alveolar and systemic levels of pro- and anti-inflammatory mediators in various animal models and in patients with ALI or ARDS ***(Ranieri et al., 1999).***

In contrast, mechanical ventilation with moderate to high levels of PEEP and low tidal volumes has been suggested to prevent tidal collapse and overdistention of lung units. This lung-protective ventilatory strategy has been shown in patients with ALI and ARDS to assure adequate gas exchange, decrease levels of intra-alveolar and systemic mediators, and improve outcome ***(Stuber et al., 1999).***

Although the most obvious clinical abnormalities in ARDS are referable to the lung, the most common cause of death is dysfunction of other organs, termed multiple organ dysfunction syndrome (MODS). MODS is often irreversible, with mortality ranging from 60% to 98%.To date, there is neither an effective treatment for MODS nor an effective means for preventing its onset ***(Esteban et al., 2002).***

Survival in patients with respiratory failure who required mechanical ventilation for more than 12 hours was 69% and depended not only on factors present when initiating mechanical ventilation but mainly on the development of complications, changes in monitored variables, and patient management during the subsequent course ***(Behrendt, 2000).***

ETIOLOGY AND PATHOPHYSIOLOGY OF ACUTE RESPIRATORY DISTRESS SYNDROME

Definition

In 1998, the American European Consensus Conference (AECC) on acute respiratory distress syndrome (ARDS) defined ARDS as "a syndrome of inflammation and increased permeability that is associated with a constellation of clinical, radiologic, and physiologic abnormalities that cannot be explained by, but may coexist with, left atrial or pulmonary capillary hypertension ***(Bernard et al., 1998).***

Hallmarks of the syndrome have classically been described as:

1. Hypoxemia with a PaO_2/FiO_2 ratio $\leq$ 300 for acute lung injury (ALI) or PaO2/FiO2 ratio $\leq$ 200 for ARDS.
2. New patchy, diffuse, bilateral pulmonary infiltrates on chest X-ray
3. Low pulmonary compliance
4. Normal left ventricular filling pressures: pulmonary capillary wedge pressure (PCWP) < 18 mmHg **(Pechulis et al., 2010).**

Although the AECC criteria have been widely used in daily practice and in clinical research, they have often been criticized and questioned, as the clinical criteria for ARDS reflect non specific functional abnormalities of the respiratory system rather than a precise structural anomaly. The typical anatomical feature of ARDS is diffuse alveolar damage (DAD), but the correlation between clinical criteria of ARDS and DAD is not well established ***(Esteban et al., 2004).***

An expanded definition of ARDS was presented by **Murray et al. (1998)**The authors include a semi-quantitative method for scoring acute lung injury derived, in part, from criteria used by other investigators. The scoring involves a four-point system: (1) the impairment of oxygenation is quantified by the ratio of arterial oxygen tension to the fraction of inspired

oxygen (PaO_2/FIO_2); (2) the chest X-ray is scored on the four-point system; if the chest X-ray is clear, then no points are assigned; one to four points are assigned for consolidation in the four lung zones; (3) the respiratory compliance may be measured by applying an end expiratory hold or plateau and the plateau pressure minus the positive end-expiratory pressure (PEEP) divided by the tidal volume delivered gives the static pulmonary compliance; (4) the PEEP level: the PEEP applied may influence arterial oxygenation and provides some indication of the severity of respiratory failure

***Table (1-1)*: Scoring acute lung injury**

	Value	Score
1. Chest radiograph score		
No alveolar consolidation	–	0
Alveolar consolidation in one quadrant	–	1
Alveolar consolidation in two quadrants	–	2
Alveolar consolidation in three quadrants	–	3
Alveolar consolidation in all four quadrants	–	4
2. Hypoxemia score		
PaO_2/FIO_2	≥ 300	0
PaO_2/FIO_2	225-299	1
PaO_2/FIO_2	175-224	2
PaO_2/FIO_2	100-174	3
PaO_2/FIO_2	< 100	4
3. Respiratory system compliance score (when ventilated)		
Compliance	≥ 80 ml/cmH,O	0
Compliance	60-79 ml/cmH,O	1
Compliance	40-59 ml/cmH2O	2
Compliance	20-39 ml/cmH,O	3
Compliance	≤ 19 ml/cmH,O	4
4. PEEP score (when ventilated)		
PEEP	≤ 5 cmH,O	0
PEEP	6-8 cmH2O	1
PEEP	9-11cmH2O	2
PEEP	12-14 cmH,O	3
PEEP	≥ 15 cmH,O	4
The final value is obtained by dividing the aggregate sum by the number of components that were used:		
No lung injury		0
Mild-to-moderate lung injury		0.1-2.5
Severe lung injury (ARDS)		> 2.5

From Murray et al. (1998)