Novel Pharmacological Interventions for Acute Respiratory Distress Syndrome

ESSAY

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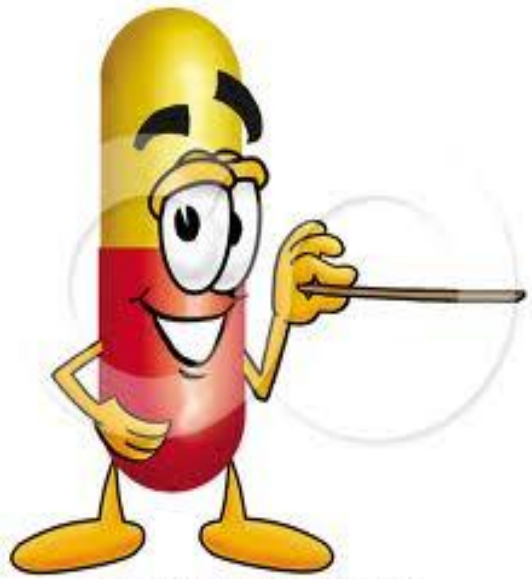
ARDS overview

Advances in supportive management



Novel Pharmacological Interventions for ARDS

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Abbreviation

5-HT	5-hydroxy tryptamine
AECC	American–European Consensus Conference Committee
ALI	acute lung injury
Ang1	angiopoietin-1
APACHE	Acute Physiology and Chronic Health Evaluation
APRV	Airway pressure release ventilation
ARDS	acute respiratory distress syndrome
AT1	alveolar cell type 1
BAL	bronchoalveolar lavage
BiPAP	biphasic positive airway pressure ventilation
COX-2	cyclooxygenase-2 enzyme
CPAP	continuous positive airway pressure
CT	Computed Tomography
CVP	central venous pressure
DAD	diffuse alveolar damage
ECMO	Extracorporeal Membrane Oxygenation
EN	Enteral nutrition
ENaC	epithelial Na^+ channel
EPA	eicosapentaenoic acid
ES	embryonic stem cells
ET-1	endothelin-1
FACTT	Fluid and Catheter Treatment Trial
FDA	food and drug administration
Fio_2	fractional inspired oxygen
GLA	γ-linolenic acid
GM-CSF	Granulocyte Monocyte- colony stimulating factor
GOCA	Gas exchange, Organ failure, Cause, Associated disease
HAPE	high altitude pulmonary edema
HFOV	High-frequency oscillatory ventilation
HMGCoA	3-hydroxy-3-methyl-glutaryl-CoA
IL-1	Interleukin

IL-1ra	IL-1 receptor antagonist
iNOS	inducible nitric oxide synthetase
IV	Intravenous
KGF	Keratinocyte growth factor
KL-6	Krebs van den Lungen-6
LIP	Lower inflection point
LIS	lung injury score
LL-37	Cathelicidin-related antimicrobial peptides
LPS	Lipopolysaccharide
MAP	Mean arterial pressure
MMP-9	Matrix metalloproteinase-9
mPaw	mean airway pressure
MSC	mesenchymal stem cells
NAC	N-acetylcysteine
NIH	National Institutes of Health
NO	nitric oxide
OL	open lung
OLB	Open lung biopsy
OP	oscillatory pressure amplitude
P/V curve	Pressure / volume curve
PAF	platelet activating factor
Pao_2	Arterial oxygen tension
PAOP	Pulmonary artery occlusion pressure
PCV	Pressure controlled ventilation
PEEP	positive end expiratory pressure
PIP	peak inspiratory pressure
PUFA	polyunsaturated fatty acid
Q_c	capillary perfusion
rhAPC	recombinant human activated protein C
RM	recruitment maneuver
SAPS	Simplified Acute Physiology Score
SpO_2	oxyhemoglobin saturation by pulse oximetry.
TBLB	transbronchial lung biopsy
TF	Tissue Factor
TNF-α	tumor necrosis factor α

t-PA	tissue plasminogen activator
UIP	Upper inflection point
V_A	alveolar ventilation
VAP	ventilator-associated pneumonia
VT	Tidal volume
VWF	von Willebrand factor

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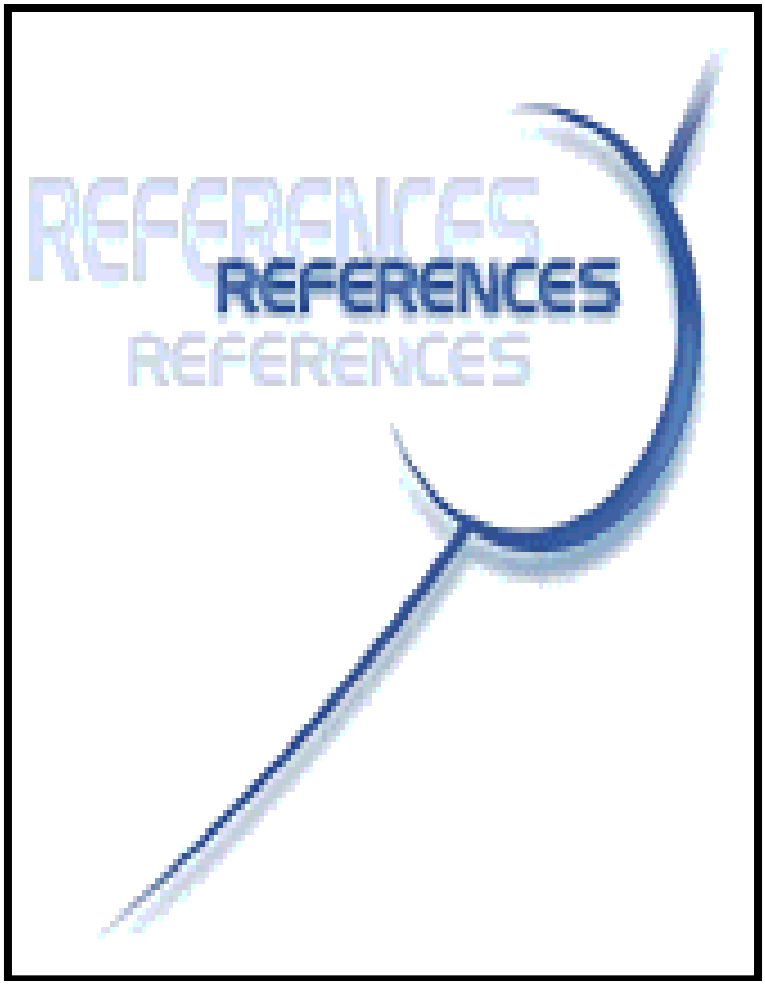
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Summary


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Introduction

The definition of Acute respiratory distress syndrome (ARDS) developed by the American- European Consensus Committee (AECC) on ARDS in 1994 consisted of 4 main components: (1) acute onset of respiratory distress within 7 days of initial inciting injury; (2) hypoxemia; (3) bilateral infiltrates on frontal chest radiographs; and (4) pulmonary capillary wedge pressure (PCWP) of 18 mm Hg or less, or no clinical evidence of left atrial hypertension. This last requirement resulted in the exclusion of patients with congestive heart failure (CHF). The degree of hypoxia divided patients into 2 groups: patients were considered to have acute lung injury (ALI) if their P_aO_2/ F_iO_2 ratio was 300 mm Hg or less whereas patients were considered to have ARDS (a subset of ALI) if the ratio was 200 mm Hg or less. ARDS/ALI can arise from direct injury to the lung parenchyma or from indirect systemic insults transmitted to the lung by the pulmonary circulation. Although more than 60 conditions have been associated with ARDS, the most frequent cause is sepsis, followed by pneumonia and aspiration. **(Rubenfeld et al, 2005)**

Over the past two decades, a variety of interventions and intensive care strategies have been used in treating patients with ALI/ARDS. The current standard of clinical care for ALI/ARDS includes mechanical ventilation with lung protective strategies, coupled with judicious fluid management, adjunct nutritional support, and specific treatment of any known underlying cause of injury or disease. The only intervention to date that has clearly showed a survival benefit in controlled studies the adoption of low tidal volume ventilation strategies (6–8 ml/kg bodyweight). **(ARDSnet, 2000)**

An individual pharmacologic agent may in fact be effective in mitigating its intended target of pathology, but benefits to survival and other long term clinical outcomes may be obscured by remaining aspects of pathology. All these considerations complicate the design and analysis of clinical trials and reduce their resolving power. In general, evaluating therapies in ALI/ARDS requires multi-center studies of substantial size, with patient populations and outcome variables controlled with as much focus as possible. **(Krishnan et al, 2008)**