Effectiveness and Outcome of Methylprednisolone versus Hydrocortisone in Treatment of Acute Respiratory Distress Syndrome (ARDS)

THESIS
For Partial Fulfilment of Master Degree in General Intensive Care.

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2019

بسم الله الرحمن الرحيم

وقُلِ اعْمَلُوا فَسَيَرَى اللَّهُ عَمَلَكُمْ وَرَسُولُهُ وَالْمُؤْمِنُونَ

صدق الله العظيم

سورة التوبة آية (١٠٥)

Acknowledgment

First and foremost, all praise to God, who has graced me with everything I've ever asked for and more.

I find it difficult to express –in one page–my gratitude and sincere feelings to my supervisors and all those who offered me help and advice during laying down the manuscript of this thesis. Your contribution will always be remembered.

I would like to express my deepest respect to ***Prof. Dr. Khaled Mohamed Maghawry****, Professor of anesthesiology, intensive care and pain management, Faculty of Medicine-Ain shams University for his continuous advice, support and guidance.*

I would also like to express my deep gratitude to ***Dr. Rania Magdy Mohammed Ali,*** *Assistant professor of anesthesiology, intensive care and pain management, Faculty of Medicine-Ain shams University for her encouragement, sincere guidance, and patience during accomplishment of this work.*

I would also like to express my deep gratitude to ***Dr. Rania Hassan Abdel Hafiez,*** *Lecturer of anesthesiology, intensive care and pain management, Faculty of Medicine-Ain shams University for her encouragement, sincere guidance, and patience during accomplishment of this work.*

Finally and mostly, special thanks to my parents, family and fellow colleagues for their endless support, patience, and forbearance during my work.

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List of Abbreviations

AECC : American-European Consensus Conference.

ALI : Acute lung injury.

Ang-1 : Angiopoietin-1.

Ang-2 : Angiopoietin-2.

ARDS : Acute respiratory distress syndrome.

AT1 : Alveolar type 1.

CPAP : Continuous positive airway pressure.

CVP : Central venous pressure.

ECMO : Extracorporeal membrane oxygenation.

ELSO : Extracorporeal life support organization

FACT : Fluid and Catheter Treatment.

FDG : 2-fluoro-2-deoxy-D-glucose.

FV : Femoral vein.

GDF-15 : Growth differentiation factor-15.

HR : Heart rate.

IL-1β : Interleukin 1beta.

IVC : Inferior vena cava.

KGF : Keratinocyte growth factor.

LIS : Lung Injury Score.

LTVV : Low tidal volume ventilation.

MAP : Mean arterial pressure.

MOF : Multiple organ failure.

NETs : Neutrophil extracellular traps.

nmMLCK : Non-muscle myosin light chain kinase.

PAMPs : Pathogen-associated molecular patterns.

PEEP : Positive end expiratory pressure.

PHV : Permissive hypercapnic ventilation.

PMN : Polymorphonuclear neutrophils.

PRRs : Pattern recognition receptors.

RA : Right atrium.

RIJV : Right internal jugular vein.

S1P : Sphingosine-1 phosphate.

SD : Standard deviation.

sICAM-1 : Soluble intercellular adhesion molecule.

SOFA : Sequential Organ Failure Assessment.

SPO_2 : Oxygen saturation.

SVC : Superior vena cava.

TNFα : Tumor necrosis factor alpha.

VA ECMO : Veno-arterial ECMO.

VE-cadherin: Vascular endothelial cadherin.

VEGF : Vascular endothelial growth factor.

VV ECMO : Veno-venous ECMO.

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Abstract:

Introduction: Acute respiratory distress syndrome (ARDS) is the clinical manifestation of severe acute lung injury. It is characterized by dyspnea, profound hypoxemia, diffuse bilateral infiltrates secondary to non-cardiogenic pulmonary edema on chest radiography, and decreased lung compliance. It occurs most frequently in the setting of sepsis, aspiration of gastric contents, trauma, or multiple blood transfusions. ARDS places a significant burden on the healthcare system, with an estimated prevalence of 7% of ICU admissions and hospital mortality rate of 50%.Pulmonary and systemic inflammations are the pathophysiologic hallmarks of this syndrome, and activation of the glucocorticoid receptor in pulmonary and circulating cells is an essential step in restoring homeostasis. Provision of supplemental oxygen, lung rest, and supportive care are the fundamentals of therapy. Acute respiratory distress syndrome frequently requires endotracheal intubation and mechanical ventilation. A low tidal volume and low plateau pressure ventilator strategy is recommended to avoid ventilator-induced injury. The use of low-dose corticosteroids was associated with improved mortality and morbidity outcomes without increased adverse reactions. The aim of this study is to compare the effectiveness of methylprednisolone to hydrocortisone in improvement of PaO2/FiO_2 ratio, reduction of inflammatory marker, reduce duration of mechanical ventilation, reduce duration of intensive care unit stay and decrease of mortality rate in critical ill patients with ARDS.

Introduction

Acute respiratory distress syndrome (ARDS) is a critical syndrome caused by heterogeneous etiologies, and is characterized by acute progression of respiratory symptoms and signs, bilateral diffuse infiltrates on chest imaging, and severe hypoxemia. The severity of ARDS is associated with poor prognosis and higher mortality, and, by the Berlin definition, diagnostic hypoxemia is defined as decreased arterial PaO_2/FiO_2 ratio with parameters of 201-300 mmHg for mild ARDS, 101-200 mmHg for moderate ARDS, and ≤100 mmHg for severe ARDS ***(Lee, 2017).***

ARDS is a severe lung disease characterized by a very complex pathophysiology, involving not only the respiratory system but also nonpulmonary distal organs. The predominant cause of death in ARDS is not severe hypoxemia, which is one of the defining criteria of ARDS, but multiple organ failure (MOF). Despite improvements in outcome due to lung protective ventilation strategies using low tidal volumes, the mortality rate from acute respiratory distress syndrome (ARDS) remains unacceptably high, ranging from 34% to 64% ***(Del Sorbo and Slutsky, 2011).***

Strong association has been established between dysregulated systemic inflammation and progression of acute respiratory distress syndrome (ARDS). In ARDS patients, glucocorticoid receptor-mediated down regulation of systemic inflammation is essential to restore homeostasis, decrease morbidity and improve survival and can be significantly enhanced with prolonged low-to-moderate dose glucocorticoid treatment. A large body of evidence supports a strong association between prolonged glucocorticoid treatment-induced down regulation of the inflammatory response and improve pulmonary and extrapulmonary physiology ***(Schwingshackl and Meduri, 2016)***.

Aim of the Work

The aim of this study was to compare the outcome and effectiveness of hydrocortisone to methylprednisolone in treatment of acute respiratory distress syndrome in critically ill adult patients.

Acute Respiratory Distress Syndrome

A) Background:

Since World War I, it has been recognized that some patients with nonthoracic injuries, severe pancreatitis, massive transfusion, sepsis, and other conditions develop respiratory distress, diffuse lung infiltrates, and respiratory failure, sometimes after a delay of hours to days. In 1967, ***Ashbaugh and his colleagues*** were described 12 such patients, using the term "adult respiratory distress syndrome" to describe this condition ***(Ashbaugh et al., 1967)***

Before research into the pathogenesis and treatment of this syndrome could proceed, it was necessary to formulate a clear definition of the syndrome. Such a definition was developed in 1994 by the American-European Consensus Conference (AECC) on acute respiratory distress syndrome (ARDS). The term "acute respiratory distress syndrome" was used instead of "adult respiratory distress syndrome" because the syndrome occurs in both adults and children ***(Bernard et al., 1994)***.

ARDS was recognized as the most severe form of acute lung injury (ALI), a form of diffuse alveolar injury. The AECC defined ARDS as an acute condition