Low dose steroids in early severe acute respiratory distress syndrome

Thesis
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Abstract

Introduction: Acute respiratory distress syndrome places a significant burden on the health-care system, with an estimated prevalence of 7% of ICU admissions and an unacceptable hospital mortality rate of 50%. Pulmonary and systemic inflammation 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. While changing the ventilator settings to low tidal volume reduces systemic inflammation with a favorable impact on survival, a concomitant anti-inflammatory pharmacologic intervention should lead to a more rapid resolution of ARDS and earlier extubation. **Methods:** Our study was conducted on thirty patients admitted in the Critical Care Department, Cairo University Hospital with proven diagnosis of **Early Severe ARDS.** The studied population was divided into two groups: ***Group I***: Twenty patients were subjected to methylprednisolone treatment protocol plus conventional management for ARDS and ***Group II***: Ten patients were kept on conventional management for ARDS. All the studied population were subjected to full history taking, detailed clinical examination, full laboratory investigations, pan-cultures, APACHE II scoring system, MODS score on days(1 and 7),LIS on days (1,2,3,5and 7) ,serial chest radiographs ,invasive arterial line insertion, pulmonary artery catheter insertion, serial measurements of CRP on days (1,3,5 and 7) ,testing of adrenal function, lung protective strategy protocol and evaluation of the outcome as regards 1-point reduction in LIS or successful extubation ,duration of MV, length of ICU stay and ICU mortality.

Results: In our study , there were significantly lower values of ***MODS score*** on day (7) in group I compared to group II patients (1.8$\pm$1.1 vs 2.7$\pm$0.9 respectively, P value: 0.022),also we found that there was statistically significant decline in ***LIS*** in day (7) in group I compared to group II patients (1.925+0.815 vs 2.85+0.5676 respectively ,P value: 0.003) and a significant lower ***CRP*** values on day 7 in group I compared to group II patients was found (8.35+7.741mg/dL vs22.1 +16.394 mg /dL, p value:0.004) respectively. By day 7: The response of the two groups clearly diverged; the methylprednisolone-treated group had a statistically significant difference as regards ***a)1-point reduction in LIS*** (70% of patients in group I vs 20% of patients in group II , P value: 0.028) and ***b) successfully extubation***(11 patients in group I vs 1 patient in group II,P value: 0.048), moreover the treated patients had a statistically significant decrease in ***number of days of MV*** of (11.15 + 7.08 in group I vs 20.9+9.08 in group II respectively, P value 0.004). Our study did not demonstrate any significant difference in the incidence of ***new infection, neuromuscular weakness, uncontrolled hyperglycemia and GIT bleeding complications*** between the treatment and control groups,(p values: 0.7945,0.954 , 0.446 and 0.954) respectively. Also no significant difference in the ***length of ICU stay*** and ***ICU survival*** between group I and group II patients was found (P value: 0.846 and 0.06) respectively.

Conclusions*:* The use of low-dose corticosteroids provides evidence of efficacy in ***EARLY SEVERE ARDS*** (accelerated resolution of systemic and pulmonary manifestations of ARDS with significant reduction in duration of mechanical ventilation) with less adverse effect.

Key words: *ARDS; duration of mechanical ventilation; glucocorticoid treatment; infections; systemic inflammation*

Abbreviations: *APACHE _ acute physiology and chronic health evaluation; Fio2 _ fraction of inspired oxygen; LIS _ lung injury score; MODS _ multiple organ dysfunction syndrome; PEEP _ positive end-expiratory pressure4*

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List Of Abbreviations

ABGs	arterial blood gases
ACM	alveolocapillary membrane
ACTH	adrenocorticotropic hormone
AFC	alveolar fluid clearance
AIDS	Acquired immunodeficiency syndrome
ALI	Acute lung injury
AP-1	activator protein-1
APACHE II	Acute Physiology and Chronic Health Evaluation
APS	Acute physiology score
ARDS	acute respiratory distress syndrome
ARDSexp	extra pulmonary causes of ARDS
ARDSp	pulmonary causes of ARDS
BAL	Bronchoalveolar lavage
CBG	corticosteroid-binding globulin
CMV	controlled mandatory ventilation
CNS	central nervous system
CO2	Carbon diaoxid

COX-2	cyclooxygenase-2
CRH	Corticotropin-releasing hormone
CRP	C-reactive protein
CT	Computed tomography
CXC	Chemokine
CXCR4	chemokine receptor 4
DAD	diffuse alveolar damage
DIC	disseminated intravascular coagulation
DM	Diabetes Mellitus
ECMO	Extracorporeal membrane oxygenation
EMG	electromyography
ENaC	epithelial sodium channel
ETT	endotracheal tube
FDA	Food and Drug Administration
FiO2	fraction of inspired oxygen
GC	glucocorticoid
GI	Gastrointestinal
GIT	Gastrointestinal Tract

GREs	glucocorticoid responsive elements
GRs	glucocorticoid receptors
GRα	glucocorticoid receptor α
HDR	host defense response
HFV	high-frequency ventilation
HIR	host inflammatory response
HPA	hypothalamic-pituitary-adrenal
hsp	heat-shock protein
ICU	intensive care unit
IFNγ	interferon
IgE	Immuneglobuline E
IGF-I	insulin-like growth factor-I
IL	interleukin
IL-1ra	interleukin receptor antagonist
iNO	inhaled nitric oxide
K	Potassium
LIS	Lung injury score
Ly	lung lymphatics

MLIS	Murray lung injury score
MMR	measles, mumps, rubella
MODS	multiple organ dysfunction syndrome
MV	Mechanical ventilation
Na	Sodium
NAC	N-acetylcysteine
NF-κB	nuclear factor-κB
NIH	National Institutes of Health
NO	nitric oxide
P value	probability value
PA	Pulmonary artery
PaO2	partial pressure of arterial oxygen
PBL	peripheral blood leukocytes
PBW	predicted body weight
PCO2	partial pressure of arterial carbon diaoxid
PCWP	Pulmonary Capillary Wedge Pressure
PEEP	positive end-expiratory pressure
PF ratio	partial pressure of arterial oxygen/fraction of inspired oxygen

PGE1	Prostaglandin E1
PHV	permissive hypercapnic ventilation
PLA2	phospholipase A2
PMN	Polymorphsnuclearleukocyte (neutrophil)
PV	Pressure volume
QO2	oxygen delivery
RA	rheumatoid arthritis
RAP	right atrial pressure
RM	recruitment maneuver
RR	Respiratory rate
SD	Standard Deviation
SLE	Systemic lupus erythromatosis
SpO2	oxyhemoglobin saturation
SRC-1	steroid receptor coactivator-1
TIA	Transien Ischemic attack
TNF	Tumor necrosis factor
VA/Q	ventilation–perfusion ratio
VALI	ventilator-associated lung injury

VILI	ventilator-induced lung injury
Vo2	oxygen uptake
V_t	Tidal Volume
vWF	von Willebrand factor

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