Diagnostic Value of Bronchoalveolar Lavage and level of Nuclear Factor-Kappa B in Acute Lung Injury in Critically Ill Children

Thesis

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Summary and Conclusion

The present study aimed at estimation of NK-B level in broncho-alveolar fluid using fiber-optic bronchoscope (FOB) in critically ill pediatric patients with ALI and evaluation of its diagnostic value.

The current study included 20 critically ill pediatric patients on mechanical ventilation, with ALI, admitted to Ain Shams PICU. It included 20 non –ALI mechanically ventilated children as control group.

Patients with past history of chronic pulmonary disorder, patients with cardiac lesion, COPD and sarciodosis were excluded from the present study. All patients underwent full clinical examination, chest AP view X-ray, laboratory investigation including; complete blood count, CRP, and arterial blood gases.

Broncho-alveolar lavage by fiber-optic bronchoscope was used to study NK-B level in BAL in ALI patients and mechanically ventilated control group (non ALI- group). NK-B was assayed in BAL by ELISA.

ALI affects males (70 %) more than females (30 %) and the difference is not significant and bronchopneumonia is the most common cause as a direct injury to the lungs (40%). Moreover NK-B level in broncho-alveolar lavage of patients was highly significant elevated (Mean = 0.58 ug/ug nuclear

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List of Abbreviations

AIDS : Acquired Immunodeficiency Virus Syndrome
a.a : Amino Acids
ALI : Acute lung injury
ALIS : Acute lung injury score
AP : Anteroposterior
ARDS : Adutl (Acute) Respiratory distress syndrome
AP-1 : Activator Protein-1
ACM : Alveolar capillary membrane
AECC : American- European Consensus Committee
APRV : Airway Pressure Release Ventilation
ARF : Acute Respiratory failure
BAL : Bronchoalveolar lavage
BiPAP : Biphasic Airway Pressure
CT : Computerized tomography
CPAP : Continous Positive Airway Pressure
CBP : CREP Binding Protein
CREB : cAMP-Responsive Element-Binding Protein
CTD : C-Terminal Domain
DAD : Diffuse alveolar damage
DNA : Deoxyribonucleic Acid
ECCO2 : Extracorporeal Carbon dioxide removal
ECMO : Extracorporeal Membrane Oxygenation
ELISA : Enzyme –linked Immunosorbent Assay
EPCS : Endothelial Progenitor Cells
Fio2 : Fraction of inspired oxygen
FRC : Function Residual Capacity
FOB : Fiberoptic bronchoscope
HFOV : High- Frequency Oscillatory Ventilation
HFV : High –Frequency Ventilation
HIF : Hypoxia- induced Factor
HLH : Helix-Loop-Helix

IκB : Inhibitor-Kappa B
IBD : Inflammatory Bowel Disease
ICAM : Intracellular Adhesion Molecule
IFNγ : Interferon Gamma
Ig : Immunoglobulin
IKK : Inhibitor-Kappa-B Kinase
I:E ratio : Inspiratory to Expiratory time ratio
ICU : Intensive Care Unit
IL : Interleukin
INO : Inhaled Nitric Oxide
IRV : Inverse Ratio Ventilation
iNOS : Inducible Nitric Oxide Synthase
IRAK : Interleukin-1 Receptor Associated Kinase
IRF : IFN Regulatory Factor
KD : Kinase Domain
LPS : Lipopolysaccharides
LBP : Lipopolysaccharide –Binding Protein
LIS : Lung Injury Score
LZD : Leucine Zipper Domain
MAP : Macrophage Activating Protein
MAPK : Mitogen Activated Protein Kinase
MEKK : MAPK Extracellular Kinase Kinase
MV : Mechanical ventilation
NAECC : North American- European Consensus Committee
NO : Nitric Oxide
NEMO : NFκB Essential Molecule
NF-κB : Nuclear Factor-Kappa B
NF-AT : Nuclear Factor of Activated T Cell
NIK : NF-κB Inducing Kinase
PaCO2 : Partial pressure of arterial carbon dioxide
PaO2 : Partial pressure of oxygen
PEEP : Positive end expiratory pressure
PEEPi : Intrinsic PEEP
PFC : Perfluorocarbon

PC-PLC : Phosphatidylcholine –Specific Phospholipase C
PICU : Pediatric Intensive Care Unit
PIP : Peak Inspiratory Pressure
PLV : Partial Liquid Ventilation
PAMPs: Pathogen-Associated Microbial Patterns
PKA : Protein Kinase A
RHD : Rel Homology Domain
RIP : Receptor Interacting Protein
RSV : Respiratory Syncytial Virus
SARS : Severe Acute Respiratory Syndrome
SD : Standard Deviation
SODD : Silence of Death Domain
TAB : TAK-Associated Binding Protein
TAD : Transactivating Domain
TAK : Transforming Growth Factor B Activated Kinase 1
TCR : T-Cell Receptor
TIR : Toll/ IL-1 Receptor/ Resistance
Tk : Tyrosine Kinase
TRALI : Transfusion –Related Acute Lung Injury
TLR : Toll-Like Receptor
TNF : Tumour Necrosis Factor
TNFR : Tumour Necrosis Factor Receptor
TRADD : TNFR-Associated Death Domain
TRAF2 : TNFR Associated Factor
USA : United States of America
V/Q ratio : Ratio of alveolar ventilation to pulmonary capillary blood flow
VT : Tidal Volume

Introduction

Acute lung injury (ALI) is a clinical syndrome that describes a single common end point; severe injury to the alveolar capillary membrane and the development of protinacious edema ***(Suratt et al., 2006).***

Acute respiratory distress syndrome (ARDS) is a severe form of acute lung injury that results from inflammation causing major changes in lung architecture and functions ***(Timmons et al., 2006).***

Incidence of acute lung injury (ALI) in ventilated patients reach up to 16.1%, more than half of these patients may develop ARDS. Observational studies report 50 - 60% mortality ***(Brun-Busson et al., 2004).***

Acute lung injury (ALI) is most often seen as part of systemic inflammatory process particularly systemic sepsis where the lung manifestations parallel to those of other tissues. Widespread destruction of the capillary endothelium, extravasations of protein rich fluid and interstitial edema, with subsequent alveolar basement membrane damage. Hence inflammatory cells and fluid sweep into the airspaces, stiffening the lungs and causing ventilation-perfusion mismatch ***(Ware et al., 2000).***

NF-κB (nuclear factor kappa-light-chain-enhancer of activated B cells) is a protein complex that controls the

transcription of DNA. NF-κB is found in almost all animal cell types and is involved in cellular responses to stimuli such as stress, cytokines, free radicals, ultraviolet irradiation and bacterial or viral antigens. NF-κB plays a key role in regulating the immune response to infection. Conversely, incorrect regulation of NF-κB has been linked to cancer, inflammatory and autoimmune diseases, septic shock, viral infection ***(Tian et al., 2003).***

Bronchoalveolar lavage (BAL) is the collection of airway linning fluid through fiberoptic bronchoscopy and has been regarded as the "Liquid biopsy" of the lung ***(Flori et al., 2003).***

Fiberoptic bronchoscopy is the prodcedure of choice to obtain uncontaminated bronchoalveolar lavage fluid.The technique is safe, minimally invasive and reveals sepcific information to the extent that it can even replace lung biopsy ***(Luh and Chiang, 2007)***.

Aim of the work

The aim of this work is to study the diagnostic value of Nuclear Factor-Kappa B level in BAL fluid by fiberoptic bronchoscope in children with acute lung injury.