SOLUBLE TRIGGERING RECEPTOR EXPRESSED ON MYELOID CELL-1 (TREM-1) IN PEDIATRIC PATIENTS WITH VENTILATOR-ASSOCIATED PNEUMONIA

Thesis

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List of abbreviations

ALI	Acute lung injury
ARDS	Acute respiratory distress syndrome
BAL	Broncho-alvealar lavage
Ca^{2+}	Calcium
Cath	Catheter
CD1a	Cluster of diffrentiation 1a
cDNA	Complementary DNA
COPD	Chronic obstructive pulmonary disease
CPIS	Clinical pulmonary infection score
CRP	C-reactive protein
CTSS	Closed tracheal suctioning system
DAP12	Adapter protein 12
DCs	Dendritic cells
ERK	Extracellular signal-regulated kinases
ET	Endotracheal tube
ETA	Endotracheal aspirate
FEV	Forced expiratory volume
FiO2	Fraction of Inspired Oxygen
FMLP	N-formyl-methionylleucyl-phenylalanine
GER	Gastro-esophageal reflux
GNB	Gram negative bacilli
Hb	Haemoglobin
HCO3	Bicarbonate
HH	Heated humidifiers
HIV	Human Immunodeficiency Virus
HME	Heat and moisture exchanger
HMG-1	High mobility group -1
ICU	Intensive care unit
IgG	Immunoglobulin G

IL-1a	Interlukin 1a
IL-1b	Interlukin-1b
IL-8	Interlukin-8
ITIM	Immunoreceptor Tyrosine based Inhibition Motif
LES	Lower esophageal sphincter
LPS	Lipopolysacharide
MAb	Monoclonal antibody
MCP-1	Monocyte chemoattractant-1
MCP-3	Monocyte chemoattractant-3
MRSA	Methicillin resistant staphylococcus aureus
MSSA	Methicillin sensitive staphylococcus aureus
MV	Mechanical ventilation
NIMV	Noninvasive mechanical ventilation
NK	Natural killer
NKp44	Natural killer p44
OTSS	Open tracheal suctioning system
Pao2	Partial Pressure of Oxygen in Arterial Blood
PCo2	Partial carbon dioxide tension
PEEP	Peak end expiratory pressure
PICU	Paediatric intensive care unit
PRISM	Pediatric risk of mortality score
PSB	Protected specimen brush
ROC	Receiver Operator Chaacteristics curve
SD	Standard deviation
SDD	Selective digestive decontamination
SSD	Subglottic secrtions drainage
TBB	Transbronchial biopsy
TLC	Total leucocytic count
TLRs	Toll-like receptors
TNF-a	Tumor necrotising factor-a
TREM-1	Triggering receptor expressed on myloid cell 1

TREM-2	Triggering receptor expressed on myloid cell -2
TREM-3	Triggering receptor expressed on myloid cell-3
VAP	Ventilator associated pneumonia

Introduction

Ventilator associated pneumonia (VAP) is a common and highly morbid condition in the intensive care unit, affecting up to 27% of mechanically ventilated patients***(Guide lines., 2005)***

Several risk factors have been reported to be associated with VAP, including the duration of mechanical ventilation, and the presence of chronic pulmonary disease, sepsis, and acute respiratory distress syndrome. ***(Jejeriana E et al., 2006)***

Mortality rates in patients with VAP range from 20 to 50% and may reach more than 70% when the infection is caused by multi- resistant and invasive pathogens. Therefore, this complication of mechanical ventilation requires a prompt diagnoses and adequate antibiotic treatment. ***(Heyland D K et al., 1999)***

Management of ventilator-associated pneumonia needs to balance the avoidance of unnecessary antibiotic overuse with the provision of adequate initial empiric therapy ***(Vidaur et al., 2005)***

The detection of the causative organism is imperative for guiding an appropriate therapy ***(Joanas et al., 2001)*** .Triggering receptor expressed on myeloid cells (TREM-1) is a member of the immunoglobulin super family***. (Papazian L et al., 1995)***

TREM-1 mediates the acute inflammatory response to microbial products. the human tissues infected with bacteria are infiltrated with neutrophils and monocytes that express high levels of TREM-1.TREM-1 is also shed by the membrane of activated phagocytes, and can be found in a soluble form in body fluids***.(Croce MA et al.,2006)***

The inflammatory response during pneumonia is a complex process. The knowledge of this response may be of clinical importance in determining more efficacious therapy. ***(Croce MA et al., 2006)***.

Aim of the study

The aim of this study is to evaluate the utility of (TREM-1) in the diagnosis of ventilator-associated pneumonia (VAP) in broncho-alveolar lavage (BAL) fluid.

Ventilator-Associated Pneumonia

Definition:

Ventilator-associated pneumonia (VAP) is nosocomial pneumonia that has developed in patients who are receiving mechanical ventilation.

VAP is divided into early onset pneumonia which occurs within 48 to 72 hours after tracheal intubation, it often results from aspiration, which complicates the intubation process. ***(Chaster J et al; 2007)***

VAP that occurs after this period is considered late-onset pneumonia, which is usually caused by antibiotic resistant pathogens (eg:oxacillin resistant Staphylococcus aureus, Pseudomonas aeruginosa, and enterobacter species)***.(Chaster J et al; 2007).***

Incidence:

Ventilator-associated pneumonia affects 8 to 20% of patients. Several risk factors have been reported to be associated with VAP, including the duration of ventilation, sepsis, acute respiratory distress syndrome (ARDS),

chronic pulmonary disease, and neurological disease***(Alvaro Rea-Neto et al; 2008).***

Mortality:

The mortality rates in patients with VAP range from 20 to 50% and may reach more than 70% when the infection is caused by multi-resistant and invasive pathogens ***(Alvaro Rea-Neto et al; 2008)***

The incidence of VAP-attributable mortality is difficult to quantify due to the possible confounding effect of associated conditions, but VAP is thought to increase the mortality of the underlying disease by about 30%. VAP is also associated with considerable morbidity, including prolonged ICU length of stay, prolonged mechanical ventilation, and increased costs of hospitalization. ***(Heyland et al;1999)***.

Etiology:

Etiologic agent of VAP may differ according to patients, units, hospitals or countries, nevertheless, comorbid conditions, length of hospital stay and exposition of antimicrobials are the most important factors determining the etiologic agent ***(Torres et al; 2001)***.