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ORIGINAL ARTICLE

Serum endocan role in diagnosis and prognosis of ventilator associated pneumonia

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KEYWORDS

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Abstract Ventilator-associated pneumonia (VAP) is a complication in as many as 28% of patients who receive mechanical ventilation. Studies have consistently shown that a delay in diagnosis and treatment increases the mortality risk.

Aim of the work: The aim of this work is to elucidate the role of the serum endocan in the diagnosis and the prognosis of ventilator associated pneumonia.

Methods: Forty-two VAP patients, 20 non VAP ICU (on mechanical ventilation) admitted patients and 20 healthy control subjects of similar age and sex were included in the study. Endocan levels in serum samples were measured in all subjects.

Results: There was a highly statistically significant difference (p value <0.001) between VAP patients on one side and non VAP-ICU patients and healthy control subjects on the other side regarding the mean values of endocan. Also, the mean values of endocan were statistically significantly higher ($p < 0.001$) among the dead VAP group than the survivor VAP group. There was a high statistically positive correlation (p value <0.001) between mortality prediction scores (APACHE II ($R = 0.549$), CRIP ($R = 0.599$) and SOFA ($R = 0.517$)) and endocan serum levels.

Conclusions: This study found increased endocan serum levels among VAP patients. We suggest a role for endocan in the diagnosis and prediction of the prognosis of VAP patients.

Introduction

Ventilator-associated pneumonia (VAP) is pneumonia that develops 48 h or longer after mechanical ventilation and is given by means of an endotracheal tube or tracheostomy. Ventilator-associated pneumonia (VAP) results from the invasion of the lower respiratory tract and lung parenchyma by microorganisms. Intubation compromises the integrity of the oropharynx and trachea and allows oral and gastric secretions to enter the lower airways [1].

Ventilator associated pneumonia (VAP) is a complication in as many as 28% of patients who receive mechanical ventilation. The incidence of VAP increases with the duration of mechanical ventilation. Estimated rates are 3% per day for the first 5 days, 2% per day for days 6–10, and 1% per day after day 10 [2].

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The crude mortality rate of VAP is 27–76%. Studies have consistently shown that a delay in starting appropriate and adequately dosed antibiotic therapy increases the mortality risk. One of the causes of the high mortality rate is the diagnostic delay [1,3,4].

Unlike community-acquired pneumonia, it may be difficult to determine whether pneumonia has developed in a hospitalized ventilator-dependent patient. Symptoms and signs usually are not conclusive. Although the plain chest roentgenogram remains an important component in the evaluation of hospitalized patients with suspected pneumonia, it is most helpful when it is normal and rules out pneumonia. Microscopy evaluation and culture of tracheal secretions and/or expectorated sputum are also frequently inconclusive for patients clinically suspected of having pneumonia, because the upper respiratory tract of most patients in the ICU is colonized with potential pulmonary pathogens, whether or not parenchymal pulmonary infection is present [5,6].

Endocan is a novel endothelium derived soluble dermatan sulfate proteoglycan (PG) [7,8]. It is encoded by the ESM1 gene [9,10]. This gene is mainly expressed in the endothelial cells in human lung and kidney tissues. The expression of this gene is regulated by cytokines, suggesting that it may play a role in endothelium dependent pathological disorders [11].

Sepsis and inflammation have associated endothelial dysfunction ranging from vasodilation, edema to coagulopathy, ischemia, and organ failure. Since inflammatory mediators (IL-1, TNF-α) induce endocan expression, blood levels of this soluble PG may closely reflect the presence and severity of inflammation as well as the response to therapy [10]. De Freitas Caires et al. have recently described elevated blood levels of cathepsin G-cleaved endocan in patients with sepsis. This 14 kDa circulating protein (p14) is the fragment of endocan specifically cleaved by cathepsin G, a neutrophil-derived serine protease [12]. In another study, Scherpereel et al. observed that circulating endocan levels in blood was related to the severity of sepsis and also reflected the outcome of the patients [13].

Aim of the work

The aim of this work is to elucidate the role of the serum endocan in the diagnosis and the prognosis of ventilator associated pneumonia.

Subjects and methods

This study was conducted at the ICU of our university hospitals. Consent was taken from each included subject. The study included 3 groups of subjects (see Table 1):

Group 1: It included 42 VAP patients that were admitted to the ICU. The mean age was 58.09 ± 13.07. There were 27 (64.28%) males and 15 (35.72%) females.

Group 2: It included 20 non VAP ICU admitted patients (on mechanical ventilation). The mean age was 56.90 ± 10.54. There were 12 (60%) males and 8 (40%) females.

Group 3: It included 20 healthy control subjects. The mean age was 53.85 ± 11.26. There were 13 (65%) males and 7 (35%) females.

The three groups were matched for age and sex (p value >0.05).

All subjects included in this study underwent the following:

1. Complete history taking and physical examination.
2. Chest X-ray examination.
3. Complete blood picture (CBC), C reactive protein (CRP), liver and kidney functions tests
4. Arterial blood gases analysis (ABGs).
5. Acute Physiology and Chronic Health Evaluation II (APACHE II) score was calculated for patient groups only.
6. The Sequential Organ Failure Assessment score (SOFA) was calculated for patient groups only.
7. The Clinical Pulmonary Infection Score (CPIS) was calculated for patient groups only
8. Measurement of endocan serum levels: This was done in all subjects included in this study. Blood samples were taken and the sera were separated and stored at −80 °C for further endocan analysis. Endocan levels were determined with the commercially available enzyme-linked immunesorbent assay (ELISA; LUNGINNOV Systems, Lille, France) [12]. For VAP patients endocan measurement was done on the first day of diagnosis (for comparing with other subject groups) and then repeated on the 7th day of diagnosis.

Pneumonia was classified as VAP if it occurred after 48 h of mechanical ventilation and was not incubated before the initiation of the mechanical ventilation. Early-onset VAP was defined as that occurring during the first 4 days on mechanical ventilation, whereas VAP develops thereafter was classified as late-onset [8]. A diagnosis of pneumonia was suspected when a new, persistent infiltrate, consolidation, cavitation or pleural effusion was seen on chest X-rays and at least two of the following were observed: a body temperature below 36 °C or above 38 °C; a white blood cell count lower than 4000/mm^3 or higher than 11,000/mm^3; and macroscopically purulent tracheal aspirate. Tracheal aspirate was classified as purulent or nonpurulent after visual inspection. Tracheal aspirate for quantitative culture had been obtained before antimicrobial treatment was started. Tracheal aspirate cultures yielding $\geqslant 10^5$ CFU/ml were considered positive. We calculated the clinical pulmonary infection score (CPIS). Patients were assumed to have VAP when the CPIS was >6. Patients received a diagnosis of VAP only after other medical conditions to which the presenting symptoms, signs or radiological findings could be attributed had been ruled out. For all patients in whom the clinical suspicion of VAP was confirmed, empirical antimicrobial therapy was started immediately and modified after culture results if needed. Patients were followed until resolution of pneumonia or death [9].

Exclusion criteria

Any patient that had any one of the following was excluded from this study: (1) Age below 18 years; (2) The development of pneumonia within 48 h of the beginning of mechanical ventilation; (3) Evidence of bacterial infection elsewhere; (4) Immuno-suppression; (5) Expected early death.