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Procalcitonin and C-reactive Protein for Early Detection of Ventilator Associated Pneumonia in Intubated and Mechanically Ventilated Patients

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ABSTRACT

Introduction

Ventilator associated pneumonia has very high mortality. Inadequate antimicrobial treatment is an import determinant of mortality in ventilator associated mortality. Antimicrobial treatment is usually guided by culture and sensitivity which requires at least 12 to 48 hours. In many recent studies Procalcitonin and C-reactive protein, alone or in combination, has shown a promising predictive ability to detect sepsis. The aim of this study is to find the ability of procalcitonin and C-reactive protein to predict ventilator associated pneumonia.

Methods

All the mechanically ventilated patients were included except patients with AIDS, neutropenia and if the patient had procalcitonin level more than 0.6 ng/ml. All the patient had procalcitonin and C-reactive protein done daily from the day of intubation till seventh day of intubation. Broncho-alveolar aspirate sample was sent on third day of intubation. Statistical analysis was done to find sensitivity and specificity of both the biomarkers to predict ventilator-associated pneumonia.

Results

C-reactive protein was high initially and decreased gradually over seven days. Procalcitonin was low and undetectable initially, highest on the third day of intubation and gradually deceased over the next following days. On the third day, Procalcitonin was found to be highly sensitive and specific to detect ventilator associated pneumonia compared to C-reactive protein.

Conclusions

Compared to C-reactive protein, procalcitonin is a good biomarkers for predicting early pneumonia in intubated and ventilated patients in ICU that can guide us in escalating antibiotics before the availability of culture and sensitivity

Keywords: procalcitonin; c-reactive protein; ventilator-associated pneumonia; intubated and mechanically ventilated.

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INTRODUCTION

Ventilator-associated pneumonia (VAP) is defined as pneumonia occurring more than 48 hours after endotracheal intubation and the initiation of mechanical ventilation. The mortality rate for VAP ranges from 24% to 50% and can reach 76% in some specific settings or when lung infection is caused by high-risk pathogens. A body of evidence shows that inadequate antimicrobial treatment is an important determinant of mortality. Adequacy of antimicrobial therapy is usually assessed on the third day of treatment, on the basis of clinical parameters and microbiological identification. However, blood culture, including identification and drug sensitivity testing, requires at least 12–48 hour, therefore early-stage diagnosis is very important. In the past two decades, procalcitonin has been adopted for early-stage diagnosis. Procalcitonin is a precursor hormone of calcitonin. It was found that when the body is stimulated by an inflammatory response, especially bacterial infection, different cells in multiple organs secrete procalcitonin.[1,2] Many studies have shown that procalcitonin has an excellent predictive ability for sepsis.[3] Clinically, the combination of the C-reactive protein level and white blood cell count is commonly used as a basis for determining infection , although there is a lack of solid evidence. [4]This study focused on ability of procalcitonin, and C-reactive protein for predicting positive endo- tracheal aspirate culture in intubated and mechanically ventilated adult patients in ICU.

METHODS

A descriptive cross sectional study was conducted in the Department of Anesthesiology, College of Medical Sciences and Teaching Hospital, Bharatpur-10, Chitwan. Ethical approval was taken from institutional review committee of College of Medical Science (COMSTH-IRC) (Ref No. COMSTH-IRC-2021/44/01). Informed and written consent was taken from all the patients' prior data collection. Data of the patients was collected from intensive care unit (ICU) of the College of Medical Sciences. Sample size was calculation was based on study conducted by oksuz et al.[5] The expected proportion of population were positive culture as observed by oksuz et al.[5] by taking 5% margin of error and 95% confidence interval. The optimum sample size after calculation was 148 but this study was conducted among 150 patients. All the intubated and mechanically ventilated patients with age more than 18 years were include in this study. Patients who had previous diagnosis of AIDS or neutropenia below 500 cells/ml and PCT value > 0.5 on the day of intubation were excluded from this study. Pneumonia was considered ventilator- associated when it occurred after 48 hours of mechanical ventilation and was judged to not have been incubating before starting mechanical ventilation. VAP was considered early- onset when it occurred during the first four days of mechanical ventilation and late-onset when it developed five or more days after the initiation of mechanical ventilation. The enrolled patients were follow-up with daily Procalcitonin (PCT) and C- reactive protein (CRP) along with the other routine investigations. The first day of intubation and ventilation is considered as D0 (day of intubation) followed by D1 (first day after intubation), D2, D3, and so on. Potentially clinical relevant cut-off points for procalcitonin were chosen at the level of the functional sensitivity of the test (0.6 ng/ml) and CRP was evaluated at a cut-off point of 20 mg/l. The Procalcitonin (PCT) and C- reactive protein (CRP) reports were collected till the D7. On the third day after intubation, the endo-tracheal aspirate collected and sent to the central Lab for culture sensitivity. And the report was followed –up in next 72 hours. All patients received empirical antimicrobial therapy on D0. The

choice of antibiotics and changes rested solely with the critical care team or primary service caring for the patient. Mechanical ventilation, physiotherapy and airway management were performed in accordance with a standard protocol in all patients. Data of the patients was collected using pre designed questionnaire. Collected data was checked for completeness, accuracy and then entered and analyzed using SPSS-20. Data was analyzed using descriptive statistical tools. In the descriptive statistics for categorical variables frequency and percentage was calculated. While for continuous variable mean and standard deviation was be calculated.

RESULTS

In this study, the total participants were 150 patients. The demographical data of the study population is as shown in (Table 1).

Table 1. Demographical distribution of study patients (n = 150).

Patient characteristics	Values
Age (years)	
Mean±SD	40.81±17.45
Gender	
Male	116(77.33)
Female	34(22.67)
Weight (kg)	
Mean±SD	63±19

In this study, we observed that CRP was significantly high on the day of intubation in over all participants which gradually decreased over seven days, as shown in (Figure 1). In over all participants, procalcitonin was below the cutoff value in most of the participants on the day of intubation, which was seen to be significantly high in third day after intubation and gradual decline was observed over the next days as shown in (Figure 2).

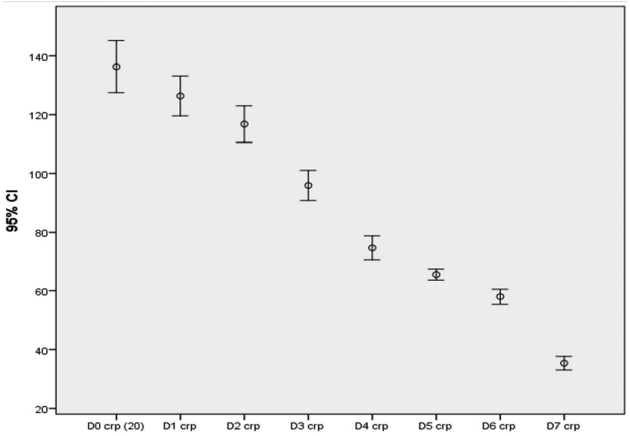

Figure 1. Pattern of observed CRP in mechanically ventilated patients.

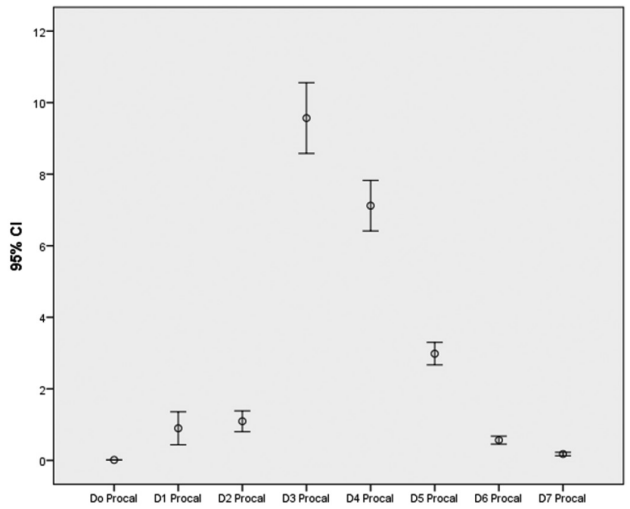

Figure 2. Pattern of observed Procalcitonin in mechanically ventilated patients.

Sensitivity and specificity of CRP and procalcitonin on third day after intubation to broncho-alveolar lavage culture was calculated using chi square test as shown in table no.2. Compared to CRP, Procalcitonin was found to have higher sensitivity and specificity.

Table 2. Sensitivity and specificity of blood markers (n=150).

Parameter	Sensitivity	Specificity
CRP	40.8%	26.7%
Procalcitonin	89.2%	76.7%

DISCUSSION

In the past two decades, procalcitonin has been adopted for early-stage diagnosis. Procalcitonin is a precursor hormone of calcitonin. It was found that when the body is stimulated by an inflammatory response, especially bacterial infection, different cells in multiple organs secrete procalcitonin.[1,2] Many studies have shown that procalcitonin has an excellent predictive ability for sepsis.[3] C-reactive protein is a marker of acute inflammation and is associated with non-specific inflammatory responses by the human body to infection or trauma. Blood C-reactive protein levels rapidly rise during such events. However, few studies have focused on the discriminative power of elevated lactate levels in blood to predict bacteremia in the literature. Sepsis is not easy to detect in the early phase, as the clinical manifestation could be latent or an exacerbation of a pre-existing condition, resulting in diagnostic difficulty.[6] However, blood culture, including identification and drug sensitivity testing, requires at least 12–48 h; therefore, early-stage diagnosis is very important. The results of the tests for procalcitonin, C-reactive protein, and lactate can be obtained within 1 h, which may significantly shorten the time of decision-making for prescribing appropriate antibiotics if bacteremia is highly suggested by the results of the above tests, either singly or in combination. The results of the tests for procalcitonin, C-reactive protein, and lactate can be obtained within 1 h, which may significantly shorten the time of decision-making for prescribing appropriate antibiotics. This study focused on the differences in the performances of procalcitonin and C-reactive protein to predict broncho-alveolar lavage culture.

In a study by Mohamed et al , they observed that survivors showed a continuous and significant decrease of CRP ratio during the first week of antibiotic therapy.[7] Similarly, in a study done by Seligman et al, they suggested that measurement of PCT and CRP at onset and on the fourth day of treatment can predict survival of VAP patients and a decrease in either one of these marker values predicts survival.[8] In our study, we observed the pattern of blood CRP and Procalcitonin in mechanically ventilated patients. We observed that initial CRP levels were very high, which reflects the level of sepsis or trauma sustained by the individual requiring mechanical ventilation. CRP level over a period of time, appropriate antibiotics and nursing care, was found to gradually decrease. Whereas Prolactin levels were initially low and most of the time undetectable, and increased to higher than cutoff value (0.6 ng/ml) over few days. Highest prolactin levels were observed on the third day after intubation. Prolactin level gradually decreased to lower level on consecutive days.

Muller et al suggested that serum calcitonin precursor concentrations are more sensitive and are specific markers of sepsis as compared with serum C-reactive protein, interleukin-6, and lactate levels.[9] Similarly, Diaz et al suggested that PCT provides additional information on the risk of VAP and Inclusion of PCT in diagnostic algorithms could improve their effectiveness.[10] In our study, we observed that prolactin was highly sensitive and specific to BAL culture. This reflects that prolactin level can be used to predict ventilator associated pneumonia in its early phase.

In a study done by Povoa et al, they observed that daily C-reactive protein measurements after antibiotic prescription were useful in the identification, as early as day 4, of ventilator-associated pneumonia patients with poor outcome.[11] They also suggested that identification of the pattern of C-reactive protein response to antibiotics was useful in the recognition of individual clinical course, improving or worsening, as well as of the rate of improvement.

In a Study by kumar et al., they observed that, when the clinical pulmonary infection score (CPIS) exceeded 6, there was an association with the presence of pneumonia in mechanically ventilated patients which was confirmed by ET tube aspiration culture.[12] They also suggested that serum CRP is an easy, available and cheap test so serial rise in titres of CRP in mechanically ventilated patients along with CPIS helps in the early diagnosis of pneumonia and aggressive treatment to prevent mortality and morbidity. In our study, we also observed that sensitivity and specificity of CPR to BAL culture was significantly low. This observation suggests that though CRP is a good marker of trauma and sepsis, but with early use of appropriate antibiotics in post trauma and post –surgery cases, may not be a good predictor of ventilator associated pneumonia.

CONCLUSIONS

This study conclude that procalcitonin is a good biomarkers for predicting early infection (VAP) in intubated and ventilated patients in ICU which can guide us before the availability of culture and sensitivity, and proper use of antibiotics over empirical use of antibiotics, hence decrease the multidrug resistance as well as improve overall out come of patients. CRP is initially high in trauma, post-surgery and sepsis cases which usually receive early antibiotics. This is followed by gradual decrease with time and proper treatment, and does not correlate with the timing of onset of VAP.

Recommendation

We recommend to use procalcitonin as a daily routine investigation especially in intubated and mechanically ventilated patients for early detection of ventilator-associated pneumonia.

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Conflict of Interest: The authors declare that no competing interests exist.

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