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Original Research Article

Procalcitonin-Based Strategy for Antibiotic Discontinuation in Ventilator-Associated Pneumonia

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Abstract:

Background: This study evaluated the role of procalcitonin-guided antibiotic discontinuation in patients with ventilator-associated pneumonia in an intensive care setting.

Methods: A prospective, controlled study was conducted in the Intensive Care Unit of the 108 Military Central Hospital from August 2019 to April 2020. Forty-five adult patients with ventilator-associated pneumonia were randomly allocated to a procalcitonin-guided group (n = 22) or a control group receiving standard guideline-based therapy (n = 23). In the intervention group, antibiotics were discontinued when serum procalcitonin decreased to <0.5 ng/mL or by ≥80% from the peak value. Clinical characteristics, microbiological findings, antibiotic duration, and clinical outcomes were compared between groups.

Results: Baseline clinical and microbiological characteristics were comparable between groups ($p > 0.05$), with Gram-negative bacteria predominating. The duration of antibiotic therapy was significantly shorter in the procalcitonin-guided group than in the control group (10.68 ± 2.33 vs. 14.91 ± 4.98 days, $p < 0.05$), and antibiotic-free days within 28 days after ventilator-associated pneumonia onset were significantly longer (16.32 ± 4.11 vs. 12.00 ± 5.78 days, $p < 0.05$). No significant differences were observed between groups in duration of mechanical ventilation, length of intensive care unit stay, in-hospital mortality, or recurrence of pneumonia (all $p > 0.05$).

Conclusions: Procalcitonin-guided antibiotic discontinuation significantly reduced antibiotic exposure without adversely affecting major clinical outcomes in ventilator-associated pneumonia. This strategy appears feasible and safe in the intensive care unit and may support antibiotic stewardship efforts in Vietnam.

Keywords: ventilator-associated pneumonia; procalcitonin; antibiotic stewardship; intensive care unit; antibiotic discontinuation.

INTRODUCTION

Ventilator-associated pneumonia is one of the most frequent and severe infections in intensive care units, leading to prolonged mechanical ventilation, extended length of stay, increased healthcare costs, and higher mortality [1, 2]. Prompt initiation of empirical broad-spectrum antibiotics is essential; however, excessive duration of antibiotic therapy contributes to antimicrobial resistance, drug-related adverse effects, and disruption of host microbiota [3]. Consequently, strategies that safely shorten antibiotic exposure without compromising clinical outcomes are a major focus of contemporary antibiotic stewardship programs in critical care settings.

Procalcitonin is a biomarker increasingly used to guide antibiotic discontinuation in patients with suspected or confirmed bacterial infections. It is the precursor of calcitonin and is normally produced in the thyroid at very low concentrations [4]. During systemic bacterial infections, procalcitonin is released in large amounts from extra-thyroidal tissues under stimulation by pro-inflammatory cytokines such as interleukin-1β and tumor necrosis factor-α, as well as bacterial endotoxins [2, 5]. In contrast, procalcitonin levels are less elevated in viral infections or non-infectious inflammatory conditions, making it relatively specific for bacterial causes. Serial measurements of procalcitonin reflect the dynamic course of infection, as levels decline with effective treatment, thereby supporting clinical decisions on antibiotic discontinuation, particularly in intensive care and respiratory infection settings [6-9].

Evidence from randomized controlled trials and meta-analyses indicates that procalcitonin-guided antibiotic discontinuation can reduce antibiotic exposure by approximately 25–27% or shorten treatment duration by one to two days in intensive care patients, including those with ventilator-

associated pneumonia, without increasing mortality, treatment failure, or adverse outcomes [8, 10-12]. These strategies are most effective when applied to guide discontinuation rather than initiation of antibiotics, and some studies suggest a modest reduction in short-term mortality when adherence to procalcitonin algorithms is high [10, 12, 13]. Nevertheless, procalcitonin is not a perfect marker, as levels may be influenced by severe systemic inflammation or organ dysfunction, and its diagnostic accuracy for initiating antibiotics in ventilator-associated pneumonia remains limited [14-17].

Despite growing international evidence, data on the role of procalcitonin-guided antibiotic discontinuation in Vietnamese patients with ventilator-associated pneumonia are scarce. Therefore, this study aims to evaluate the role of procalcitonin in antibiotic therapy with respect to the duration of antibiotic treatment and other clinical outcomes in an intensive care unit setting in Vietnam.

MATERIALS AND METHODS

Study Population

A total of 45 patients diagnosed with ventilator-associated pneumonia were enrolled in this study at the Intensive Care Unit of the 108 Military Central Hospital between August 2019 and April 2020. Eligible patients were randomly allocated into two groups. The intervention group comprised 22 patients whose antibiotic therapy was guided by serum procalcitonin levels and discontinued when procalcitonin concentrations decreased to below 0.5 ng/mL or showed a reduction of at least 80% from the peak value (PCT group). The control group included 23 patients who received antibiotic therapy in accordance with current clinical guidelines without reference to serum procalcitonin values.

Inclusion and Exclusion Criteria

Patients aged 18 years or older who met the diagnostic criteria for ventilator-associated pneumonia as defined by the 2016 guidelines of the Infectious Diseases Society of America and the American Thoracic Society were eligible for inclusion [1]. Written informed consent was obtained from all patients or their legal representatives prior to enrollment, and complete clinical and laboratory data required for the study were available. Patients were excluded if they had been intubated or mechanically ventilated at another institution, died or were discharged before discontinuation of antibiotic therapy, or were transferred from the intensive care unit to another department during treatment.

Study Design and Procedures

This was a prospective, longitudinal study with a control group, conducted using a convenience sampling method. Following the diagnosis of ventilator-associated pneumonia according to the IDSA/ATS 2016 criteria, patients were randomly assigned to either the PCT-guided group or the control group [1]. In the PCT group, serum procalcitonin levels were measured serially, and antibiotic therapy was adjusted and discontinued according to the predefined procalcitonin thresholds. In the control group, patients received empiric antibiotic therapy based on standard treatment guidelines, with subsequent modifications guided by microbiological culture and antimicrobial susceptibility results. All patients were monitored throughout their ICU stay for clinical status, laboratory and paraclinical parameters, treatment response, and outcomes. Intensive care physicians were informed of the study protocol at the time of ventilator-associated pneumonia diagnosis and participated in patient management according to the assigned treatment strategy.

Data Management and Statistical Analysis

Data were collected using standardized case report forms and managed in a dedicated database. Statistical analyses were performed using SPSS software version 20.0. Appropriate statistical tests were applied to compare antibiotic duration and clinical outcomes between the two study groups, in accordance with the study objectives.

Ethical Considerations

All patients and their family members were fully informed about the objectives and procedures of the study prior to providing written informed consent. Participating physicians received training regarding the study aims, content, and conduct before patient enrollment. The study was approved by the Medical Ethics Committee of the 108 Military Central Hospital and was conducted in accordance with ethical principles for medical research involving human subjects

RESULTS

A total of 45 patients with ventilator-associated pneumonia were included in the analysis, comprising 22 patients in the procalcitonin-guided group and 23

patients in the control group. Baseline clinical characteristics and laboratory parameters were comparable between the two groups, with no statistically significant differences observed. These findings indicate that the two study groups were well matched at enrollment (Table 1).

Table 1. Baseline clinical characteristics and laboratory findings of ventilator-associated pneumonia patients (n = 45)

Characteristics	PCT group (n = 22)	Control group (n = 23)	p
Gender, n (%)			
Female	4 (18.2)	3 (13.0)	> 0.05
Male	18 (81.8)	20 (87.0)	
Age (years, mean ± SD)	54.41 ± 17.74	56.09 ± 22.38	> 0.05
Temperature (°C, mean ± SD)	38.33 ± 0.66	38.26 ± 0.51	> 0.05
Pulse (beats/min, mean ± SD)	99.45 ± 15.90	96.39 ± 16.81	> 0.05
Mean arterial pressure (mmHg, mean ± SD)	87.32 ± 11.48	90.00 ± 13.20	> 0.05
White blood cells (G/L, mean ± SD)	12.96 ± 6.82	12.40 ± 3.21	> 0.05
Neutrophils (%, mean ± SD)	83.15 ± 7.14	81.23 ± 6.36	> 0.05
Platelets (G/L, mean ± SD)	194.86 ± 79.36	182.39 ± 69.99	> 0.05
Chest X-ray findings, n (%)			
One-sided lesions	9 (40.9)	12 (52.2)	> 0.05
Bilateral lesions	13 (59.1)	11 (47.8)	
Diffuse infiltrates	12 (54.5)	13 (56.5)	
Localized infiltrates	10 (45.5)	10 (43.5)	
Pleural effusion, n (%)	16 (72.7)	12 (52.2)	> 0.05
CPIS (mean ± SD)	7.14 ± 2.12	7.30 ± 1.91	> 0.05
SOFA score (mean ± SD)	5.95 ± 2.01	5.83 ± 1.15	> 0.05
Serum PCT at diagnosis (ng/mL, mean ± SD)	5.51 ± 6.28	4.63 ± 5.09	> 0.05
Serum PCT at antibiotic discontinuation (ng/mL, mean ± SD)	0.39 ± 0.25	0.50 ± 0.40	> 0.05
Time to VAP onset (days, mean ± SD)	3.27 ± 1.75	3.43 ± 1.23	> 0.05

Microbiological analysis of respiratory specimens showed that Gram-negative bacteria were the predominant pathogens in both groups. Among patients with positive sputum cultures, Gram-negative organisms accounted for more than three quarters of isolates, with *Acinetobacter baumannii*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* being the most frequently identified pathogens. The distribution of causative microorganisms was similar between the procalcitonin-guided group and the control group (Table 2).

Table 2. Microbiological characteristics of sputum cultures in the two study groups

Microbiological results	**PCT group (n = 22)**	**Control group (n = 23)**
Positive cultures, n	13	18
Gram-negative bacteria, n (%)	10 (76.9)	14 (77.8)
Pseudomonas aeruginosa, n (%)	1 (7.7)	2 (12.5)
Escherichia coli, n (%)	0 (0.0)	3 (18.7)
Klebsiella pneumoniae, n (%)	4 (30.7)	4 (31.2)
Acinetobacter baumannii, n (%)	5 (38.4)	4 (31.2)
Gram-positive bacteria, n (%)	3 (24.1)	4 (22.2)
Staphylococcus aureus, n (%)	2 (15.4)	0 (0.0)
Streptococcus pneumoniae, n (%)	1 (7.7)	3 (22.2)

Regarding treatment outcomes, the duration of antibiotic therapy was significantly shorter in the procalcitonin-guided group compared with the control group. In addition, patients in the procalcitonin group experienced a significantly longer antibiotic-free period within 28 days after ventilator-associated pneumonia onset. However, no statistically significant differences were observed between the two groups with respect to duration of mechanical ventilation, length of intensive care unit stay, in-hospital mortality, or recurrence of pneumonia (Table 3).

Table 3. Treatment outcomes in the procalcitonin-guided and control groups

Outcomes	PCT group	Control group	p

	(n = 22)	(n = 23)	
Duration of mechanical ventilation (days, mean ± SD)	9.00 ± 2.74	9.87 ± 2.58	> 0.05
Length of ICU stay (days, mean ± SD)	10.86 ± 3.69	11.39 ± 3.89	> 0.05
Duration of antibiotic therapy (days, mean ± SD)	10.68 ± 2.33	14.91 ± 4.98	< 0.05
Antibiotic-free days within 28 days after VAP (days, mean ± SD)	16.32 ± 4.11	12.00 ± 5.78	< 0.05
Mortality, n (%)	3 (13.6)	3 (13.0)	> 0.05
Recurrent pneumonia, n (%)	2 (9.0)	3 (13.0)	> 0.05

DISCUSSION

This study provides an initial evaluation of procalcitonin-guided antibiotic discontinuation in patients with ventilator-associated pneumonia managed in an intensive care unit. The findings suggest that integrating serial procalcitonin measurements into clinical decision-making can support earlier discontinuation of antibiotics without adversely affecting key clinical outcomes, thereby reinforcing the potential role of procalcitonin as an adjunctive tool for antibiotic stewardship in critically ill patients.

The microbiological profile observed in this study demonstrates a clear predominance of Gram-negative pathogens in ventilator-associated pneumonia, with similar distributions between the procalcitonin-guided and control groups. This finding is consistent with the epidemiology of VAP reported in intensive care units worldwide, particularly in settings with high rates of antimicrobial resistance, where *Acinetobacter baumannii*, *Klebsiella pneumoniae*, and *Pseudomonas aeruginosa* are frequently isolated. The comparable microbiological characteristics between groups suggest that differences in treatment outcomes were unlikely to be driven by pathogen distribution, thereby strengthening the internal validity of the observed effects of procalcitonin-guided antibiotic discontinuation.

In terms of antibiotic use, the significantly shorter duration of antibiotic therapy and the longer antibiotic-free period within 28 days in the procalcitonin-guided group are in line with robust evidence from randomized trials and meta-analyses. Large pooled analyses consistently report that procalcitonin-guided strategies reduce antibiotic exposure by approximately 1.2 to 1.8 days compared with standard care, without compromising safety [13, 18-20]. These effects have been attributed to the ability of serial procalcitonin measurements to reflect resolution of bacterial infection, thereby providing clinicians with objective support to discontinue antibiotics earlier, even in critically ill patients with respiratory infections.

Despite the reduction in antibiotic exposure, no significant differences were observed between the two groups with respect to duration of mechanical ventilation, length of ICU stay, mortality, or recurrence of pneumonia. This finding is consistent with prior studies showing that procalcitonin-guided antibiotic discontinuation does not adversely affect major clinical outcomes, with most meta-analyses reporting no significant differences in ICU length of stay or ventilator duration [10, 13, 19]. Although some large studies have demonstrated a modest reduction in short-term mortality associated with procalcitonin-guided strategies, particularly in sepsis and respiratory infection subgroups [20-22], such benefits may be difficult to detect in smaller single-center cohorts. Additionally, while recent analyses have reported a slight increase in recurrent infection rates associated with procalcitonin guidance, this has not translated into higher rates of secondary infections or worse clinical outcomes [19, 20], a pattern that is consistent with the findings of the present study.

Several limitations of this study should be acknowledged. The single-center design and relatively small sample size may limit the generalizability of the findings and reduce statistical power to detect differences in secondary outcomes. In addition, although patients were randomly allocated, the use of convenience sampling and the lack of blinding may have introduced selection and performance biases. Finally, procalcitonin levels can be influenced by severe systemic inflammation or organ dysfunction, which were not explored in depth in this study and may have affected clinical decision-making.

CONCLUSION

In conclusion, this study suggests that procalcitonin-guided antibiotic discontinuation is a feasible and safe strategy for patients with ventilator-associated pneumonia in the intensive care unit, leading to reduced antibiotic exposure without negative effects on major clinical outcomes. These findings support the incorporation of procalcitonin-guided algorithms into antibiotic stewardship practices and highlight the need for larger, multicenter studies in Vietnam to further confirm the benefits and optimize implementation in routine clinical care.

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