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Clinical Efficacy and Economic Evaluation of Dynamic Procalcitonin (PCT) Monitoring in Guiding Antibiotic Course Management for Sepsis

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Abstract: ***To evaluate the clinical efficacy and health economic value of procalcitonin (PCT)-guided antibiotic discontinuation based on dynamic monitoring in ICU patients with sepsis. A prospective cohort study was conducted involving 180 sepsis patients admitted to our ICU from January 2023 to June 2024. Patients were divided into a PCT-guided group (n=90) and a conventional therapy group (n=90). In the PCT-guided group, antibiotic discontinuation was considered when the daily monitored serum PCT level fell below 0.25 ng/mL and had decreased by ≥80% from its peak, combined with clinical assessment. The conventional group followed standard clinical practice based on experience, imaging, and traditional lab markers. Outcomes including 28-day all-cause mortality, antibiotic duration, ICU and total hospital length of stay (LOS), total medical costs, incidence of antibiotic-associated adverse events, and microbiological resistance profiles were compared. No significant difference was found in 28-day mortality between the PCT-guided and conventional groups (22.2% vs. 25.6%, P>0.05). The PCT-guided group showed significantly shorter antibiotic duration [(8.5±3.2) vs. (12.1±4.5) days], ICU LOS [(10.3±4.1) vs. (13.8±5.2) days], and total hospital LOS [(18.6±6.8) vs. (22.4±7.9) days] (all P<0.01). Total medical costs were significantly lower in the PCT-guided group [(15.3±5.2) vs. (18.9±6.1) ten thousand CNY, P<0.01], primarily due to savings in antibiotic costs and ICU-related expenses. The incidence of antibiotic-associated diarrhea (including C. difficile infection) was significantly lower in the PCT-guided group (5.6% vs. 13.3%, P<0.05).***

Keywords: Procalcitonin, Sepsis, Antibiotic Duration, Clinical Efficacy.

1. Introduction

Sepsis, defined as life-threatening organ dysfunction caused by a dysregulated host response to infection, remains a leading cause of mortality in intensive care units (ICUs) worldwide [1]. It is characterized by high fatality rates and consumes substantial healthcare resources. Early recognition and prompt administration of effective antibiotic therapy are fundamental to improving outcomes in septic patients. However, the inappropriate use of antibiotics, particularly excessively prolonged courses, has emerged as a critical global public health challenge. This practice directly contributes to the rapid escalation of bacterial antimicrobial resistance (AMR), increases the incidence of drug-related adverse events, and drives up unnecessary healthcare costs. Consequently, achieving precise shortening of unnecessary antibiotic exposure while ensuring therapeutic efficacy has become a central objective in both the clinical management of sepsis and hospital Antimicrobial Stewardship Programs (ASPs) [2].

Traditional decision-making regarding antibiotic cessation has largely relied on physician experience and non-specific indicators such as patient fever resolution, white blood cell count normalization [3], and imaging improvement. These parameters are often lagging and lack specificity, frequently resulting in either unduly prolonged therapy or delayed discontinuation [4]. Identifying a biomarker capable of dynamically and specifically reflecting the severity of bacterial infection and the response to treatment is therefore crucial for achieving individualized and precise antibiotic management [5].

Procalcitonin (PCT), a precursor peptide of calcitonin, is present at very low levels in the serum of healthy individuals. During systemic bacterial infection, its concentration can rise rapidly within 2-6 hours, with the magnitude of increase positively correlating with infection severity [6]. Conversely, with effective antimicrobial treatment, PCT levels decline swiftly, benefiting from a relatively short half-life of approximately 20-30 hours. This unique kinetic profile renders PCT an ideal biomarker for guiding the diagnosis of infectious diseases, assessing severity, and monitoring therapeutic response [7]. Substantial evidence confirms that PCT outperforms traditional markers like C-reactive protein (CRP) in distinguishing bacterial from viral infections [8].

In recent years, strategies guiding antibiotic treatment duration based on dynamic PCT changes have garnered significant attention. Numerous randomized controlled trials (RCTs) and meta-analyses have demonstrated that [9], compared to standard therapy, PCT-guided strategies can significantly shorten antibiotic use in patients with community-acquired pneumonia, acute exacerbations of chronic obstructive pulmonary disease, and sepsis, without increasing treatment failure rates or mortality [10]. Reflecting this evidence, the 2016 Surviving Sepsis Campaign International Guidelines issued a weak recommendation suggesting that PCT levels may be used to support decisions to shorten the duration of antibiotic therapy in septic patients [11].

2. Materials and Methods

2.1 Study Design and Participants

This study was a single-center, prospective, non-randomized controlled observational cohort study. The study protocol was reviewed and approved by the hospital's Medical Ethics Committee. Written informed consent was obtained from all patients or their legal representatives.

2.1.1 Inclusion Criteria:

(1) Age ≥ 18 years.
(2) Meeting the diagnostic criteria for Sepsis-3.
(3) Expected ICU stay ≥ 48 hours.
(4) Initiation of systemic antibacterial therapy for suspected or confirmed bacterial infection.
(5) Complete clinical data available.

2.1.2 Exclusion Criteria:

(1) Pregnancy or lactation.
(2) Known diseases significantly affecting PCT levels, such as medullary thyroid carcinoma, small cell lung cancer, active autoimmune diseases.
(3) Antibiotic therapy for >72 hours prior to enrollment.
(4) Expected survival time < 72 hours.
(5) Voluntary discharge or abandonment of active treatment.
(6) Other conditions deemed unsuitable for participation by the investigators.

2.2 Grouping Method

Eligible patients who consented to participate were assigned to one of two groups based on the clinical team's inclination regarding the primary basis for antibiotic discontinuation decisions:

PCT-Guided Group: Clinicians agreed and were willing to follow a discontinuation suggestion protocol centered on dynamic PCT changes.

Conventional Therapy Group: Clinicians chose to decide the timing of antibiotic cessation based on traditional clinical experience, imaging (e.g., resolution on chest X-ray/CT), and conventional laboratory tests (e.g., normalized body temperature, normalized white blood cell count).

Baseline characteristics including age, gender, APACHE II score, and site of infection were comparable between the two groups at enrollment.

2.3 Interventions

2.3.1 PCT-Guided Group:

PCT Monitoring: Starting from the first day of antibiotic therapy, venous blood was collected every morning. Serum PCT levels were quantitatively measured using an electrochemiluminescence immunoassay. Discontinuation Reference Protocol (Decision support, not mandatory order): Strong suggestion to discontinue antibiotics: PCT level decreased to <0.25 ng/mL, and had fallen by ≥80% compared to the peak level during the current infectious episode, and the patient's clinical signs and symptoms of infection (e.g., fever, hemodynamics, organ function) had significantly improved or stabilized. Continue or adjust therapy: If PCT levels failed to decline or even increased, or remained persistently high (e.g., >1.0 ng/mL) with insignificant reduction, this suggested uncontrolled infection or complications, prompting re-evaluation of the infection source, pathogen, and treatment regimen. The final decision to stop antibiotics was made by the attending physician based on the overall clinical picture, incorporating but not solely dependent on the above PCT criteria.

2.3.2 Conventional Therapy Group:

Daily PCT monitoring was not mandatory. The frequency of PCT testing was determined by the attending physician based on the clinical course. The timing of antibiotic discontinuation was determined solely by the attending physician based on traditional clinical assessment, primarily referencing: afebrile for ≥48-72 hours, normalized white blood cell count and neutrophil percentage, significant resolution of infection on imaging, stable hemodynamics, and improved organ function.

2.3.3 Shared Management:

Both groups received standardized bundle care according to the Surviving Sepsis Campaign guidelines, including early fluid resuscitation, source control (e.g., drainage, debridement), and organ support. Initial antibiotic therapy was empirical and broad-spectrum, with timely de-escalation performed upon availability of microbiological culture and sensitivity results.

2.4 Outcome Measures

Primary Outcome: All-cause mortality within 28 days after enrollment. Secondary Outcomes: Clinical Efficacy: Total antibiotic duration (days), ICU length of stay (LOS, days), total hospital LOS (days), infection recurrence rate (need for antibiotic re-initiation for the same infection within 7 days of stopping), rate of new infections. Safety: Incidence of antibiotic-associated adverse events, including Clostridioides difficile-associated diarrhea (CDAD), drug-induced liver injury (ALT/AST >3 times upper limit of normal), and renal injury (serum creatinine increase >50% from baseline). Microbiological: Incidence of multidrug-resistant (MDR) organism isolation during treatment.

Health Economic: Total hospitalization cost, total antibiotic drug cost, ICU-related costs.

2.5 Statistical Analysis

Data analysis was performed using SPSS software (version 26.0). Continuous data conforming to a normal distribution are presented as mean ± standard deviation and were compared using the independent samples t-test. Non-normally distributed continuous data are presented as median and compared using the Mann-Whitney U test. Categorical data are presented as numberand compared using the Chi-square test or Fisher's exact test as appropriate. All statistical tests

were two-tailed, with a P-value of <0.05 considered statistically significant.

3. Results

3.1 Baseline Characteristics

A total of 180 patients were finally enrolled, with 90 patients in each group. There were no statistically significant differences between the PCT-guided group and the conventional therapy group in terms of age, gender, APACHE II score at admission, primary site of infection, comorbidities, or initial peak PCT level. This indicates that the baseline characteristics of the two groups were balanced and comparable. The mean age was approximately 66 years, about 56% of patients were male, and the mean APACHE II score was around 19. The most common infection site was pulmonary, followed by abdominal (about 21%). The median initial peak PCT level was around 8-9 ng/mL in both groups.

3.2 Primary Clinical Outcome

The 28-day mortality was 22.2% (20 out of 90 patients) in the PCT-guided group and 25.6% (23 out of 90 patients) in the conventional therapy group. The difference between the groups was not statistically significant. This indicates that the early discontinuation strategy guided by PCT did not increase the short-term risk of death for patients, confirming its non-inferiority in terms of safety regarding mortality.

3.3 Secondary Clinical and Economic Outcomes

3.3.1 Resource Use and Treatment Duration

The PCT-guided group demonstrated significantly better outcomes across all measures of treatment intensity and hospitalization time compared to the conventional therapy group. The average antibiotic duration was approximately 8.5 days in the PCT-guided group, significantly shorter than the 12.1 days in the conventional group, representing a reduction of about 3.6 days. Similarly, the average ICU length of stay was 10.3 days in the PCT-guided group versus 13.8 days in the conventional group, a reduction of about 3.5 days. The total hospital length of stay was also significantly shorter in the PCT-guided group, a reduction of approximately 3.8 days. All these differences were statistically significant.

3.3.2 Medical Costs

In terms of health economics, the PCT-guided group also showed a significant advantage. The average total hospitalization cost was approximately 153, 000 CNY in the PCT-guided group, significantly lower than the 189, 000 CNY in the conventional therapy group, resulting in an average saving of about 36, 000 CNY per patient. A further breakdown of costs revealed that the savings originated mainly from two sources: first, a direct reduction in antibiotic drug costs; and second, a substantial decrease in ICU-related costs, which include high expenses for ICU beds, monitoring, nursing, and advanced life support, attributable to the shorter ICU stay.

3.4 Safety and Microbiological Outcomes

3.4.1 Adverse Events:

The incidence of antibiotic-associated diarrhea was 5.6% in the PCT-guided group, significantly lower than the 13.3% incidence in the conventional therapy group. There were no significant differences between the two groups in the incidence of drug-induced liver injury or renal injury.

3.4.2 Infection Control and Resistance:

The rates of infection recurrence were 4.4% in the PCT-guided group and 5.6% in the conventional group, with no statistically significant difference. The rates of new infections were also similar between groups (6.7% vs. 7.8%). Furthermore, the proportion of patients from whom multidrug-resistant organisms were isolated during treatment showed no significant difference between the PCT-guided group (21.1%) and the conventional therapy group (23.3%).

4. Discussion

This prospective cohort study, conducted in a real-world ICU setting, validates the value of a dynamic Procalcitonin (PCT)-guided strategy for antibiotic discontinuation. The results demonstrate that a decision-support protocol centered on the criterion of "PCT <0.25 ng/mL and a reduction of ≥80% from peak level" achieves dual benefits in both clinical efficacy and health economics.

The cornerstone of this study's findings is the confirmed safety of the PCT-guided strategy. The absence of a statistically significant difference in 28-day all-cause mortality, alongside comparable rates of infection recurrence and new infections between the groups, aligns consistently with conclusions from numerous international large-scale RCTs and meta-analyses [12]. This finding is crucial as it directly addresses clinicians' primary concern that shortening antibiotic courses might lead to treatment failure [13].

The most significant benefit observed lies in the optimization of healthcare resource use. The PCT-guided group experienced an average reduction in antibiotic duration of approximately 3.6 days (about 30%), which directly and powerfully drove the shortening of both ICU and total hospital length of stay [14]. From a health economics perspective, this reduction creates a "multiplier effect." The ICU is the department with the highest concentration of personnel, equipment, technology, and consequently, cost within a hospital, with daily bed costs far exceeding those of general wards [15]. The data indicates that the saved ~3.5 ICU days constituted the major portion of the total cost savings.

Beyond direct economic savings, the PCT-guided strategy yielded important patient safety benefits by reducing unnecessary antibiotic exposure. A significant decrease in the incidence of antibiotic-associated diarrheawas observed [16]. CDAD, as a severe hospital-acquired infection, significantly prolongs hospitalization, increases treatment complexity and cost, and independently raises mortality risk. Preventing such complications is itself a form of cost savings and a core aspect

of healthcare quality. Furthermore, although no significant difference in bacterial resistance rates was observed between

the groups in this short-term study, reducing antibiotic exposure volume is the cornerstone for curbing the development and spread of Antimicrobial Resistance (AMR) [17].

The strengths of this study include its prospective design and application within a real-world ICU environment, providing efficacy and economic data relevant to the Chinese healthcare context [18]. However, its limitations must be acknowledged. First, as a single-center, non-randomized controlled study, despite efforts to balance baselines, selection bias may still exist. Second, the study did not conduct subgroup analyses based on different infection types, pathogens, or immune statuses. These factors might influence PCT kinetics and the optimal time for discontinuation [19].

This study confirms the clinical efficacy and economic benefits of dynamically monitoring procalcitonin (PCT) to guide antibiotic therapy in ICU patients with sepsis. Implementing a strategy based on a PCT level falling below 0.25 ng/mL and declining by at least 80% from its peak safely shortens antibiotic exposure by approximately 30% without increasing mortality or infection recurrence. Crucially, this approach generates significant cost savings by reducing both ICU and overall hospital length of stay, primarily by decreasing the use of high-cost intensive care resources. It also enhances patient safety by lowering the incidence of adverse events like antibiotic-associated diarrhea. To effectively integrate this strategy into clinical practice, we recommend hospitals establish standardized, institution- specific protocols for PCT monitoring and antibiotic decision-making. This requires fostering multidisciplinary collaboration among intensivists, infectious disease specialists, pharmacists, and microbiologists, supported by ongoing education and regular audit feedback for continuous quality improvement. Future developments should focus on enhancing diagnostic and prognostic precision by combining PCT with other biomarkers and leveraging artificial intelligence to analyze complex patient data for more personalized and predictive treatment guidance.

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