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ORIGINAL ARTICLE

Serum Procalcitonin Levels of Patients with Candidemia Hospitalized in Intensive Care Units

Mohammad Reza Yazdani[1], Farzin Khorvash[1], Atousa Hakamifard[1]

[1]*Infectious Diseases and Tropical Medicine Research Center, Isfahan University of Medical Sciences, Isfahan, Iran*

Objective: Fungal infections are a main reason for mortality of critically ill patients in Intensive Care Units (ICUs). Recently, fungal infections have been on rise. Lack of a specific marker for fungal infections has led to some problems in diagnosing these infections. Scant data exist on serum procalcitonin (PCT) levels in high-risk patients with invasive fungal infections, such as ICU patients. **Materials and Methods**: In this prospective study conducted in 2014–2015 in Al-Zahra Hospital, Isfahan, Iran, 64 people were investigated. The PCT levels of the patients were measured at 0, 24, 48, and 72 h as well as 7 and 14 days of the ICU stay. Moreover, a blood sample was taken from each person every 3 days and examined for positive BACTEC *Candida* fungal culture. **Results**: Nine (15%) patients had candidemia. The mean serum PCT level was not significantly different between the patients with and without candidemia at admission and 24, 48, and 72 h of the ICU stay ($P > 0.05$), but was significantly different on 7 and 14 days of the ICU stay ($P < 0.001$). **Conclusion**: This study demonstrated that the serum PCT levels increased significantly in the patients with candidemia hospitalized in ICUs. Therefore, serum PCT, as a marker, can be relied on, in addition to other symptoms and factors, for taking a decision about the initiation of treatment with antifungal drugs. Besides that, further studies with larger sample size are recommended to examine the predictive value of PCT for invasive fungal infections.

Key words: Procalcitonin, fungal infections, Intensive Care Unit

INTRODUCTION

Fungal infections are a main cause of mortality of critically ill patients hospitalized in Intensive Care Units (ICUs). Recently, these infections have been on rise. Lack of a specific marker for fungal infections has led to certain challenges facing the diagnosis of these infections. Since traditional methods, such as smear and culture, usually do not have high sensitivity and most biopsy specimen-based techniques are invasive and impractical for critically ill patients hospitalized in the ICUs, then the diagnoses are usually made clinically. This results in the low or high use of antifungal drugs.[1-5]

Therefore, the laboratory tests that diagnose these infections quickly are highly useful. Recent findings have confirmed the increase in the serum procalcitonin (PCT) levels of patients with bacterial infections.[6,7] PCT is a prohormone of calcitonin and is produced by the thyroid C cells. In septicemia, PCT is produced by the macrophages and monocytes of different organs and released into the blood flow.

Blood PCT concentration cannot be detected in healthy people and increases in people with systemic inflammation, especially bacterial infections. The mechanism through which more PCT is produced following inflammation has not yet been explained fully. It is argued that the PCT is produced by the liver and peripheral blood mononuclear cells and regulated by septicemia-associated polysaccharides and cytokines. The secretion of PCT starts within approximately 4 h of stimulation, and peak blood is achieved within about 8 h of stimulation.[8]

The information is scant on blood PCT levels in high-risk patients with invasive fungal infections, such as ICU patients. The aim of this study was to investigate the serum PCT levels of patients with invasive fungal infections in the ICUs of Al-Zahra Hospital, Isfahan, Iran.

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Corresponding Author: Dr. Atousa Hakamifard, Infectious Diseases and Tropical Medicine Research Center, Isfahan University of Medical Sciences, Isfahan, Iran. Tel: 0098-9132291573; Fax: 0098-3136604918. E-mail: a.hakamifard@med.mui.ac.ir

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MATERIALS AND METHODS

This prospective study was conducted on the ICU patients of Al-Zahra Hospital, Isfahan, Iran, in 2014–2015. The design of the study was approved by the Ethics committee of Isfahan University of Medical Sciences.

The inclusion criteria were being admitted to the ICUs, the age over 18-year-old, and the caregiver's consent to the patient's inclusion in the study. The patients who died before completion of the study (did not stay in the ICUs for at least 15 days) were excluded from the study.

The sample size required for this study was determined to be 40 people by a sample size formula to estimate the mean levels, considering the confidence interval 95%, the test power 80%, the standard deviation of PCT serum level of approximately 1, and the minimum level of significant difference (0.4) before and after the treatment. To handle possible dropouts, we included 64 patients in this study.

After making necessary arrangements, the PCT levels of the patients were measured at 0, 24, 48, and 72 h as well as seven and 14 days of the ICU stay. For this purpose, a 5-mL blood sample was taken from each patient and centrifuged. The PCT of the samples was detected by an immunoluminometric assay (Lumitest-PCT, Brahms-Diagnostica, Berlin, Germany). The PCT level of 0.1–0.5 ng/mL was considered normal, 0.5–1 ng/mL moderate, and over 1 ng/mL high. Moreover, a blood sample was taken from each patient every 3 days. A blood sample was taken from each person every 3 days and examined for positive BACTEC *Candida* fungal culture. The purpose of this study was not determination of *Candida* species. The data were analyzed by Chi-square, independent sample *t*-test, and repeated measures ANOVA in SPSS (Statistical Package for the Social Sciences, version 23.0, SPSS Inc, Chicago, Illinois, USA) software.

RESULTS

Overall, this study investigated 64 ICU patients with specified inclusion criteria. Of these patients, four patients died within the first 4 days of ICU stay and were excluded from the study. The mean age of the patients was 62.1 ± 13.4 (range: 45–82) years. Thirty-five (58.3%) patients were men and the rest women. There was no significant difference in the mean age between male and female patients (61.7 ± 13.1 and 62.6 ± 14.1 years, respectively) ($P = 0.79$).

Twenty-eight patients (46.7%) were admitted to the ICU for trauma, 7 (11.7%) for intracranial hemorrhage, 2 (3.3%) for a brain tumor, 19 (31.7%) for cerebrovascular accident, and 4 (7.6%) for lung contusion. The mean duration of the ICU stay was 16.9 ± 4.9 (8–25) days.

Nine (15%) of sixty patients had candidemia. Table 1 shows the frequency distribution of demographic and clinical data on the patients with and without fungal infection. According to the *t*-test, the mean duration of the ICU stay and ventilation of the patients with candidemia was significantly longer, but the age and gender distribution and the reason for ICU were not significantly different between the patients with and without candidemia.

During the study, seven (11.7%) patients died. Of these patients, two did not have candidemia and five had (3.9% vs. 55.6%), with a significant difference between the patients with and without candidemia ($P < 0.001$).

The mean serum PCT levels of the patients without and with candidemia were derived 2.69 ± 2.26 and 3.09 ± 0.92 unit, respectively, at admission with no significant difference ($P = 0.6$). At 24, 48, and 72 h of the ICU stay, the mean serum PCT levels of the patients without candidemia were 3.8 ± 1.37, 4.12 ± 1.03, and 3.92 ± 0.95 and in the patients with candidemia were 3.02 ± 0.49, 4.32 ± 0.35, and 4.09 ± 0.39, respectively, with no significant difference between the two groups of the patients in none of the studied points in time ($P = 0.1$, 0.56, and 0.62, respectively).

On the days 7 and 14 of the ICU stay, the mean serum PCT levels of the patients without and with candidemia were derived 4.08 ± 1.3 and 72.6 ± 0.73 and 72.3 ± 1.36 and 32.7 ± 0.72, respectively, with a significant difference between the two groups of the patients on both days ($P < 0.001$).

Repeated measures ANOVA demonstrated a significant difference in the variations in the serum PCT levels from

Table 1: The frequency distribution demographic and clinical data on the patients for candidemia

Variables	Candidemia		*P*
	Yes	No	
Age (years), mean±SD	59.9±14.6	62.5±13.3	0.6
Gender			
Male	6 (66.7)	29 (56.9)	0.58
Female	3 (33.3)	22 (43.1)	
Causes of admission to the ICU			
Trauma	4 (44.4)	24 (47.1)	0.81
Intracranial hemorrhage	1 (11.1)	6 (11.8)	
Brain tumor	0	2 (3.9)	
Cardiovascular accident	4 (44.4)	15 (29.4)	
Lung contusion	0	4 (7.8)	
Duration of the ICU stay (days)	17.9±3.9	9.5±5	<0.001
The duration of ventilation (days)	13.3±3.2	8±5.4	0.006
Death	5 (55.6)	2 (3.9)	<0.001

ICU=Intensive Care Unit; SD=Standard deviation

admission to the ICU to the day 14 of the ICU stay in each the patients with and without candidemia ($P < 0.05$) [Figure 1]. Besides that, the mean serum PCT levels of the deceased patients were significantly higher than the survived patients on the days seven and 14 of the ICU stay.

DISCUSSION

The fungal infections are a main reason for mortality in critically ill patients in the ICUs. No specific marker has made the diagnosis of fungal infections challenging. Therefore, the laboratory tests that are able to detect these infections quickly are considered highly useful. The findings on serum PCT levels of the ICU patients with invasive fungal infections are scant and inconsistent. Petrikkos *et al*., study reported low serum PCT levels in people with invasive fungal infections.[9]

Gérard *et al*. reported that the serum PCT levels were high in patients with liver transplant and candidemia.[10] Taken together, the general aim of this study was to investigate the variations in PCT, as a marker, in the ICU patients with fungal infections.

In our study, the PCT serum levels of the patients with and without candidemia were not significantly different from admission to the ICU to 72 h of the ICU stay. However, on the days 7 and 14 of the ICU stay, the PCT serum levels of the patients with candidemia were significantly higher than those without candidemia.

Serum PCT level has already been reported to be a sensitive index for assessing the effectiveness of antifungal treatments, following up the treatments for bacterial infections, and controlling postoperative infections.[11] Therefore, the significant changes in PCT levels can be considered a useful indicator of fungal infections at hospital stay. As a result, this indicator can be used for diagnosis, prognosis, and investigation of the efficiency of antifungal treatments for the patients with simultaneous an acute disease and fungal infections.

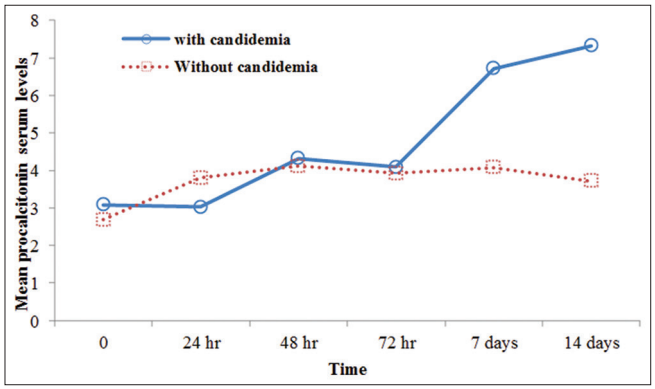

Figure 1: Comparison mean of procalcitonin serum levels from admission to the Intensive Care Unit to the day 14 of the Intensive Care Unit stay

In Hillas *et al*. study on 45 patients with ventilator-associated pneumonia; the serum PCT levels of deceased patients were significantly higher than the survived patients. Hillas *et al*. argued that these two markers were able to determine the prognosis of the ICU patients with ventilator-associated pneumonia to an acceptable level.[12]

Regarding the findings of Hillas *et al*. study and other investigations, the general conclusion can be that the serum C-reactive protein and PCT levels are high in the patients with ventilator-associated pneumonia, but these levels gradually decline as the antibiotic therapy starts and continues. As a result, these two markers can be used to determine the effect of antibiotic therapy for the patients with ventilator-associated pneumonia.

CONCLUSION

This study demonstrated that the serum PCT levels increased significantly in the patients with candidemia hospitalized in ICUs. Therefore, serum PCT, as a marker, can be used, in addition to other symptoms and factors, to take a decision about the initiation of treatment with antifungal drugs. Further studies with larger sample size are recommended to examine the predictive value of PCT for invasive fungal infections.

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Conflicts of interest

There are no conflicts of interest.

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