COMPARISON OF PROCALCITONIN VALUES OF PATIENTS IN INTENSIVE CARE UNIT WITH SYSTEMIC AND LOCALIZED BACTERIAL INFECTIONS

INCI A[1], DEMIRARAN Y[2], ERUS S[3], OCAK T[4], YAPRAK U[3], AKMAN C[4], BASTURK M[4], KALAFAT UM[4]
[1]Kanuni Sultan Suleyman Training and Research Hospital, Department of Infectious Disease and Clinical Microbiology, Istanbul - [2]Kanuni Sultan Suleyman Training and Research Hospital, Department of Anesthesiology and Intensive Care, Istanbul ,- [3]Koc University Faculty of Medicine, Department of Thoracic Surgery, Istanbul - [4]Kanuni Sultan Suleyman Training and Research Hospital, Department of Emergency Medicine, Istanbul, Turkey

ABSTRACT

***Introduction**: Intensive care unit (ICU) hospital infections are a global problem concerning the whole world. Sensitivity and specificity of parameters such as CRP (C-reactive protein), erythrocyte sedimentation rate and WBC (white blood cell), which are among the classical markers of systemic inflammation, were reported to have limited benefit in patients with these types of bacterial infections. PCT (procalcitonin) has been a focus of interest as a specific and early marker in systemic inflammation, sepsis and infections especially in recent years. In this study, we aimed to evaluate potential usability of PCT in distinction of systemic and localized bacterial infections in patients who are followed up in ICU and to compare CRP, WBC and MPV (mean platelet volume) values in patients with systemic and localized bacterial infections.*

***Materials and methods**: Totally 52 patients who were followed in Adult ICU of our hospital were included in the study. The patients were divided into two groups. Group 1 consisted of patients with growth in blood culture and systemic bacterial infection clinic. Group 2 consisted of patients with growth in phlegm, tracheal aspirate, wound and urine culture without growth in blood culture. Age, gender, growth region and growing microorganisms, simultaneously checked CRP, PCT, WBC, MPV values were recorded in follow-up form.*

***Results**: The study showed that PCT value was significantly high in systemic infections, while other parameters did not show a significant difference between the two groups. Furthermore, Acinetobacter baumannii was found to be the most common agent.*

***Conclusion**: Our study suggests that PCT value has a more valuable potential than other standard infection parameters in distinction of systemic infection and localized bacterial infection in patients who are followed in ICU. However, we believe that more comprehensive studies with a larger sampling can guide the clinicians for early diagnosis and treatment.*

***Key words**: Intensive care unit, mean platelet volume, procalcitonin, crp.*
DOI:10.19193/0393-6384_2016_1_39

***Received** May 30, 2015; **Accepted** January 02, 2016*

Introduction

Intensive care unit (ICU) hospital infections are a global problem concerning the general of the world. Infection in ICU is an important cause of morbidity and mortality. Studies on intensive care units such as antibiotic resistance and those with substantial epidemiologic data are mostly carried out in developed countries[(1)].

Infection-like clinical findings can be observed in inflammatory conditions such as trauma, pancreatitis, transplant and vasculitis[(2)].

Early diagnosis and effective treatment of bacterial infections is life-saving. Golden standard to diagnose bacterial infections is to grow the agent in culture. However, in practice, it might not always be possible to collect the culture and produce the agent and also time is required to finalize the culture. Sensitivity and specificity of parameters such as CRP (C-reactive protein), ESR (erythrocyte sedimentation rate) and WBC (white blood cell) which are among the classical markers of systemic inflammation were reported to have limited benefit in patients with these types of bacterial infections.

PCT (procalcitonin) has been a focus of interest as a specific and early marker in systemic inflammation, sepsis and infections especially in recent years[3,4].

PCT has been identified as an important indicator of bacterial infection. It is the precursor of calcitonin secreted by thyroid C cells and it has low serum levels under normal conditions. Production of the PCT is provided by endotoxins or mediators produced in response to bacterial infections such as TNF-α, IL-1, IL-6. PCT is a peptide consisting of 116 amino acids and it is not known whether it has any hormonal activity. PCT value is peaked in the first 6 hours, it returns to normal values rapidly after the infection is taken under control[5-10].

PCT serum levels shows a strong interaction with the prevalence and severity of bacterial infections. Clinical and laboratory findings such as fever, leukocytosis, elevated CRP levels and tachycardia often provide low specificity in the diagnosis of infection, whereas early diagnosis and early initiation of antibiotic treatment are quite important. Rising immediately and significantly in cases of systemic infection, PCT has risen less in localized infections. Data on PCT role in localized infections without systemic inflammatory response syndrome is very low[9,11-13].

In this study, we aimed to evaluate potential usability of PCT in distinction of systemic and localized bacterial infections in patients who are followed up in ICU and to compare CRP, WBC and MPV (mean platelet volume) values, which are other standard inflammatory parameters, in patients with systemic and localized bacterial infections.

Materıals and methods

Totally 52 patients who were followed in Adult ICU of our hospital were included in the study. The patients were divided into two groups. Group 1 consisted of patients with growth in blood culture and systemic bacterial infection clinic. Group 2 consisted of patients with no growth in blood culture, however of those with growth in phlegm, tracheal aspirate, wound and urine culture. Age, gender, growth region and growing microorganisms, simultaneously checked CRP, PCT,WBC, MPV values were recorded in follow-up form. Complete blood count has been measured using a Cell-Dyn 3700 (AbbottDiagnosticsDivision, USA), serum CRP and PCT levels have been measured using a ‘’RocheCobas 6000” device.

Values under 5 mg/dL for CRP and under 0.5 ng/mL for PCT were accepted as normal.

References ranges for the complete blood count has been determined as 3,7-10,01 x 10e3/uL for leukocyte count, 155-366 x 10e3/uL for platelet count and 6.9-10.6 fl for MPV.

Blood and other materials culture, determination of microorganism and detection of antibiotic susceptibility have been performed using BACTEC automated system.

Statistical analysis has been performed using Statistical Package for the Social Sciences (SPSS) 16.0 for Windows program, Chi-square test has been used. $P<0.05$ has been considered significant.

Results

	Group 1(n:27)	Group 2(n:25)	p
Average Age	63.81±19.91	58.08±17.91	0,28
Sex Male(n)	10/27	14/25	0,09
PCT (ng/mL)	5.57±7.12	2.54±2.99	0,04
CRP (mg/dL)	153.66±83.98	166.88±92.63	0,59
WBC(10e3/uL)	15041.85±5919.17	13638.40±7467.48	0,45
MPV(fl)	7.96±2.01	8.50±1.97	0,33

Table 1: Comparison of Demographic and Laboratory Parameters of Patients. Only PCT values were statistically significant between two groups.
PCT: Procalcitonin, CRP: C-reactive Protein, WBC: White Blood Cells, MPV: Mean Platelet Volume

A total of 52

Group 1	Microorganisms	(27 /52)
	Acinetobacter baumannii	**8(%30)**
	Pseudomonas aeruginosa	**5(%19)**
	Candida albicans	**5(%19)**
	CNS	**3(%11)**
	MRSA	**2(%7)**
	Klebsiella pneumonia	**2(%7)**
	Stenotrophomonas maltophilia	**1(%4)**
	Escherichia coli	**1(%4)**
Group 2	Microorganisms	(25 /48)
	Acinetobacter baumannii	**15(%60)**
	Pseudomonas aeruginosa	**8(%32)**
	Escherichia coli	**1(%4)**
	Klebsiella pneumonia	**1(%4)**

Table 2: Infection Types and Microorganism Distribution (n/%). Acinetobacter baumannii was found to be the most common agent in both groups.
MRSA: Methicilin-resistant Staphylococcus Aureus
CNS: Coagulase negative staphylococci

patients were enrolled in the study. In our study, PCT values were significantly higher in systemic infections, while the other parameters showed no significant differences between the two groups. Demographic characteristics and laboratory parameters of patients are seen in Table 1.

Also, it has been determined that the most common agent was Acinetobacter baumanni in both groups. The agent distribution is seen in Table 2.

Discussion

Infection is an important cause of morbidity and mortality in ICU. In cases infection is not treated appropriately, sepsis development may occur. In sepsis, as in other emergencies, beginning treatment early and effectively is very important. Therefore, definition of sepsis and initiation of treatment in early period are vital[14].

Clinical awareness, a careful physical examination, history taking and appropriate cultures are important in the diagnosis of bacterial infection. The latter, although it is the most important method, is time-consuming. Features of markers ideal for bacterial infections are to provide early diagnosis opportunities, to inform about the course and prognosis of the disease and to make treatment decisions easier. In recent years, the importance of PCT in the early diagnosis of bacterial infections has been emphasized[15].

CRP is an acute phase reactant protein produced by the liver, which increases in blood during infection and rises in the first 4-6 hours and makes peak at 48 hours. CRP falls within hours with recovery. Because of CRP levels can be elevated in many cases, it is not a single disease-specific laboratory finding[16].

Thrombocytopenia can occur in the bloodstream infections, but there is not a lot of information about changes that may occur in platelet size during bloodstream infections, changes in the MPV levels may be a marker useful for bloodstream infections[17].

In our study, PCT, CRP, WBC, MPV values were examined in systemic and localized infections. Results of this comparison showed significantly high values of PCT in systemic infections, while the other parameters showed no significant differences between the two groups.

Patients in the study of Celebi et al, has been divided into five groups as sepsis, meningitis, pneumonia, pyelonephritis and other infections. As a result it is identified that PCT is a more important marker in invasive bacterial infections, it is stated significantly high in sepsis group according to pneumonia and other infections, while CRP levels and WBC showed no significant difference[3].

In the study of Pavic et al, 25 patients were divided into two groups as systemic and localized infections and between these two groups PCT average of systemic infections was detected as 1.3 (range: 0.1-7.4) μg/L, while in localized infections it was 0.2 (range: 0.1-9.1) μg/L and it was stated that this result is significant. Between CRP and WBC values no significant difference was determined in a similar manner to our work[11].

In the study of Kim et al, in which patients with bacteremia with positive blood culture and patients with local infection were compared, PCT value was determined high in patients with bacteremia (respectively 11.9 ± 25.1 and 2.5 ± 14.7 ng/mL, $p < 0.001$). Increased PCT value can be predictive in patients with high fever to predict bacteremia, while in the study of Endo et al, it was reported that PCT can be useful for separation of sepsis and severe sepsis[18,19].

In the study of Aikawa et al, in which reproduction in blood culture was evaluated as systemic infection and reproduction in other areas was evaluated as localized infection, no significant difference ($P = 0.770$) of PCT concentrations between systemic and localized infections was reported, but PCT and CRP levels were significantly high in bacterial infections according to non-bacterial infections[20].

In the study of Luzzani et al, average concentration of PCT was determined as 1.3 μg/L (0.6-2.0) in localized infection, as 3.1 μg/L (1.4-5.2) in septic group[21].

In our country in the study of Aslan et al, 98 patients who were followed in the ICU were included in the study, PCT, CRP, ESH and WBC results were compared by dividing into two groups according to positive and negative blood cultures. In this study it was determined that there was no significant difference between the two groups in terms of PCT, CRP, ESR and WBC results[22].

Also from our country, in the study of Sumer et al on the issue, it has been showed that PCT and CRP levels are guiding for the physician for separating localized infections from healthy individuals. In the study Muller et al carried out in ICU, CRP, lactate and interleukin-6 levels were compared and it was reported that PCT level is more sensitive for

sepsis diagnosis. Also in another study on the subject it was found that PCT levels are higher in culture positive group than culture negative group and CRP level are not different between two groups[23-25].

Study	Patient Group	n	MPV	Conclusion
Tozkopran et al (28)	**Pulmonary Tuberculosis**	**82**	10.05±2.36	**There were significantly higher PDW MPV (10.05+/-2.36 vs. 8.83+/-1.47 fL)values in the active tuberculosis group,**
Qadri et al (29)	**HIV**	**234**	**8.66**	**HIV-infected women had lower MPV values than uninfected women**
Kucukbayrak et al (30)	Pulmonary hydatid cyst	72	8.07±0.83	Preoperative MPV values of the patients was found to be significantly higher than postoperative MPV values.(Mean: 8.07±0.83, 7.78±0.87, p= 0.002).
Gao et al (31)	**Septic shock death / living**	124	11.2/10.3	MPV in non-survivor group was significantly higher than that in survivor group [11.2 (10.5, 12.5) fl vs. 10.3 (9.7, 11.0) fl, relative risk (RR)=3.362, P=0.009].
Karadag et al (32)	**Pneumonia**	196	7.1 ± 0.68	Patients with CAP had lower MPV values than their healthy counterparts (7.1 ± 0.68 vs. 8.31 ± 1.2 fL p<0.001).
Inci A (33)	**CCHF**	**74**	8.98±1.13	**The mean platelet volume was**
				8.98±1.13 in CCHF group and 8.15±0.53 in the control group. There was
				a statistically significant difference between the groups(p<0.001).

Table 3: The results of some work investigating the MPV values in MPV and infectious diseases.
HIV: Human Immunodeficiency Virus
CCHF: Crimean-Congo Haemorrhagic Fever

There are studies in which usability of MPV values in sepsis and other infections is investigated. In our study MPV value was determined as 7.96±2.01 in systemic infection, as 8.50±1.97 in localized infection and no statistical significance was found. In the study by Bechii et al, it has been reported that MPV values are usable in sepsis[26]. In the study of Van der Leile J et al, it has been reported that MPV value in septic patients are higher than patients with localized infection[27]. Results of some studies in which MPV level is investigated in infectious diseases are shown in Table 3. Another study has reported strong correlation between fungal sepsis and increased MPV[34].

Because of our study was retrospective and our total number of cases was low, differences between PCT values according to agents could not be determined and this is a main flaw.

In our study we pointed-out that most frequently proliferating bacteria in both groups was Acinetobacter, this microorganism, which causes serious problems, is a well-known cause of ICU infections[35-37].

In conclusion, our study gives the impression that PCT value in patients followed in ICU has more valuable potential than other standard infection parameters to differentiate systemic infection from localized bacterial infection. However, we think that more comprehensive studies with a greater number of patients can be guiding for physicians in early diagnosis and treatment.

References

1) Ulu Kilic A, Ahmed SS, Alp E, Doganay M. *Challenge of intensive care unit-acquired infections and Acinetobacter baumannii in developing countries*. OA Critical Care 2013; 1: *1-5*.
2) Simon L, Gauvin F, Amre DK, Saint-Louis P. *Lacroix J.Serum procalcitonin and C-reactive protein levelsas markers of bacterial infection: a systematicreview and meta-analysis*. Clin Infect Dis 2004; 39: *206-17*.
3) Celebi S, Bulur N, Hacimustafaoglu M, Ozakin C, Cakir D et al. *Comparison of C-Reactive protein, Procalcitonin and Serum Amyloid-A levels in diagnosis of bacterial infection in children*. J Pediatr Inf 2013; 7: *147-56*.
4) Nargis W, Ibrahim M, Ahamed BU. *Procalcitonin versus C-reactive protein: Usefulness as biomarker of sepsis in ICU patient*. Int J Crit Illn Inj Sci 2014; 4: *195-9*.
5) Deis JN, Creech CB, Estrada CM, Abramo TJ. *Procalcitonin as a marker of severe bacterial infection in children in the emergency department*. Pediatr Emerg Care 2010; 26: *51-60*.
6) Mahajan P, Grzybowski M, Chen X, Kannikeswaran N, Stanley R et al. *Procalcitonin as a marker of serious bacterial infections in febrile children younger than 3 years old*. Acad Emerg Med 2014; 21: *171-9*.
7) Pourakbari B, Mamishi S, Zafari J, Khairkhah H, Ashtiani MH et al. *Evaluation of procalcitonin and neopterin level in serum of patients with acute bacterial infection*. Braz J Infect Dis 2010; 14: *252-5*.
8) Riedel S, Melendez JH, An AT, Rosenbaum JE, Zenilman JM. *Procalcitonin as a marker for the detection of bacteremia and sepsis in the emergency depart-*

ment. Am J Clin Pathol 2011; 135: *182-9*.
9) Schuetz P, Albrich W, Mueller B. Procalcitonin for diagnosis of infection and guide to antibiotic decisions: past, present and future. BMC Med 2011; 9: 107.
10) Mehanic S, Baljic R. The *Importance of serum Procalcitonin in diagnosis and treatment of serious bacterial ınfections and sepsis*. Materia Socio Medica 2013; 25: *277-81*.
11) Pavic M, Bronic A, Kopcinovic LM. *Procalcitonin in systemic and localized bacterial infection*. Biochemia Medica 2010; 20: *236-41*.
12) Saeed K, Ahmad N, Dryden M. *The value of procalcitonin measurement in localized skin and skin structure infection, diabetic foot infections, septic arthritis and osteomyelitis*. Expert Rev Mol Diagn 2014; 14: *47-54*.
13) Ergonul O. Crimean-Congo haemorrhagic fever. Lancet Infect Dis 2006; 6: *203-14*.
14) Gunal O, Ulutan F, Erkorkmaz U. *Prognostic Value of Procalcitonin in Sepsis Patients*. Klimik Journal 2011; 24(1): *31-5*.
15) Christ-Crain M, Muller B. *Procalcitonin in bacterial infections-hype, hope, more or less?* Swiss Med Wkly 2005; 135: *451-60*.
16) Gurler MY, Demir G, Moueminoglu F, Apaydın S, Luy N. *The effects of chemotherapy on C-reactive protein and quality of life in cancer patients*. Turkish Journal of Oncology 2014; 29: *1-10*.
17) Kitazawa T, Yoshino Y, Tatsuno K, Ota Y, Yotsuyanagi H. *Changes in the mean platelet volume levels after bloodstream infection have prognostic value*. Intern Med 2013; 52: *1487-93*.
18) Kim MH, Lim G, Kang SY, Lee WI, Suh JT, Lee HJ. *Utility of procalcitonin as an early diagnostic marker of bacteremia in patients with acute fever.* Yonsei Med J 2011; 52: *276-81*.
19) Endo S, Aikawa N, Fujishima S, Sekine I, Kogawa K et al. *Usefulness of procalcitonin serum level for the discrimination of severe sepsis from sepsis: a multicenter prospective study*. J Infect Chemother 2008; 14: *244-24*.
20) Aikawa N, Fujishima S, Endo S, Sekine I, Kogawa K et al. *Multicenter prospective study of procalcitonin as an indicator of sepsis*. J Infect Chemother 2005; 11: *152-9*.
21) Luzzani A, Polati E, Dorizzi R, Rungatscher A, Pavan R, Merlini A. *Comparison of procalcitonin and C-reactive protein as markers of sepsis*. Crit Care Med 2003; 31: *1737-41*.
22) Aslan O, Afsar, I, Demir M, Sener, AG, Koseoglu, M *Procalcitonin and C-Reactive protein levels according to blood culture results in ıntensive care unit patients*. Infectious Diseases in Clinical Practice 2014; 22: *267-70*.
23) Sumer S, Eryaman I, Aribas ET. *The Role of Procalcitonin, C-reactive protein, Interleukin-6, , Interleukin-8 and Endotoxin in the early diagnosis and fallow-up of local infections*. Nobel Med 2012; 8: *61-6*.
24) Muller B, Becker KL, Schächinger H, Rickenbacher PR, Huber PR et al. *Calcitonin precursors are reliable markers of sepsis in a medical intensive care unit*. Crit Care Med 2000; 28: *977-83*.
25) Venkatesh B, Kennedy P, Kruger PS et al. *Changes in serumprocalcitonin and C-reactive protein following antimicrobial therapy as a guide to antibiotic duration in the critically ill: a prospective evaluation*. Anaesth Intensive Care 2009; 37: *20-6*.
26) Becchi C, Al Malyan M, Fabbri LP, Marsili M, Boddi V, Boncinelli S. *Mean platelet volume trend in sepsis: is it a useful parameter?* Minerva Anestesiologica 2006; 72(9): *749-56*.
27) Van der Lelie J, Von dem Borne AK. *Increased mean platelet volume in septicaemia*. J Clin Pathol 1983; 36: *693-6*.
28) Tozkoparan E, Deniz O, Ucar E, Bilgic H, Ekiz K. *Changes in platelet count and indices in pulmonary tuberculosis*. Clin Chem Lab Med 2007; 45: *1009-13*.
29) Qadri S, Holman S, Dehovitz J, Crystal H, Minkoff H, Lazar JM. *Mean platelet volume is decreased in HIV-infected women*. HIV Med 2013; 14: *549-55*.
30) Kucukbayrak A, Oz G, Findik G, Karaoglanoglu N, Kaya S et al. *Evaluation of platelet parameters in patients with pulmonary hydatid cyst*. Mediterr J Hematol Infect Dis 2010; 2: *e2010006*.
31) Gao Y, Li L, Li Y, Yu X, Sun T, Lan C. *Change of platelet parameters in septic shock patients*. Zhonghua Wei Zhong Bing Ji Jiu Yi Xue. 2014; 26: *28-32*.
32) Karadag-Oncel E, Ozsurekci Y, Kara A, Karahan S, Cengiz AB, Ceyhan M. *The value of mean platelet volume in the determination of community acquired pneumonia in children*. Ital J Pediatr 2013; 39: *16*.
33) Inci A. *Increased mean platelet volume in patients with crimean congo hemorrhagic fever*. J Clin Anal Med 2015; 6: *1-3*.
34) Aydemir H, Piskin N, Akduman D, Kokturk F, Aktas E. *Platelet and mean platelet volume kinetics in adult patients with sepsis*. Platelets 2012; 26: *331-5*.
35) Akin A, Esmaoglu Coruh A, Alp E, Canpolat DG. *The evaluation of nasocomial ınfections and antibiotic resistance in anesthesia ıntensive care unit for five years*. Erciyes Medical Journal 2011; 33: *7-16*.
36) Sunenshine RH, Wright MO, Maragakis LL, Harris AD, Song X, Hebden J et al. *Multidrug-resistant Acinetobacter infection mortality rate and length of hospitalization*. Emerg Infect Dis 2007; 13: *97-103*.
37) Luna CM, Rodriguez-Noriega E, Bavestrello L, Guzmán-Blanco M. *Gram-negative infections in adult intensive care units of latin america and the Caribbean*. Crit Care Res Pract 2014; 2014: *480463*.

Corresponding author
TARIK OCAK, MD
Kanuni Sultan Suleyman Training and Research Hospital, Department of Emergency Medicine,
Istanbul
(Turkey)