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Original Article

Diagnostic importance of serum C-reactive protein and procalcitonin in sepsis after burn

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Abstract: Introduction: In this study, we investigated the usefulness of blood white blood cell (WBC), C-reactive protein (CRP) and Procalcitonin (PCT) levels with a clinical diagnosis of infection in patients with severe burns, with a bacterial culture (+) wound site, in patients with SIRS and sepsis. Materials and methods: In the study, 23 patients with (+) burn wound culture hospitalized in the intensive care unit of Gazi Yaşargil Training and Research Hospital Burn Center burn between January 2016 and January 2021 were analyzed. While five of these patients were showing symptoms of SIRS. Sepsis was observed in five patients. Results: From 23 patients, 18 (78.3%) were male, and 5 (21.7%) were female. The majority of our patients were lived in rural areas. The average age of patients was 1,061±17,273 years. The wound culture results of the 23 patients were (+), mostly due to *Staphylococcus aureus* in 21.7% (n=5) and *Staphylococcus epidermidis* in 21.7% (n=5). PCT and CRP results did not statistically differ in patients with sepsis, SIRS and (+) wound culture. Conclusion: The laboratory biomarkers WBC, CRP and PCT do not have a superior value in determining and monitoring infection processes in patients with serious burns.

Keywords: Burns, sepsis, white blood cell, C-reactive protein, procalcitonin

Introduction

Burn injuries occur when the integrity of the skin and other tissues is disrupted as a result of contact with heat, radiation, electricity, friction or chemicals [1]. Burn wounds are an important nutrition area for proliferations of endogenous and exogenous opportunistic organisms, which can cause infection when the infectious number reaches [2]. Infections that develop after burns are an important cause of morbidity and mortality and complicate and delay burn treatment [3]. Given that immunity changes after a burn, the risk of infection that can lead to sepsis is increased [4].

Systemic inflammatory response syndrome (SIRS) frequently occurs in large burns. Systemic inflammatory response may develop due to infection (sepsis) or non-infectious reasons [5]. The differentiation of the two clinical conditions has an important role in the regulation and monitoring of the effectiveness of the treatment. PCT, unlike the calcitonin hormone produced primarily in the thyroid gland, is a prohormone synthesised in infected organ tissues. It is known to have a stronger inflammation parameter than other blood infection markers, such as CRP [6].

The purpose of this study; after major burn trauma, we investigated the compatibility of blood WBC, CRP, and PCT levels with clinical follow-up in the diagnosis and availability in patients with a bacterial culture (+) wound site, in patients with SIRS, and in patients with sepsis. The efficacy, sensitivity, and specificity of blood WBC, CRP, and PCT levels as a diagnosis, follow-up, and prognosis marker were examined.

Material and methods

Patients who received inpatient burn treatments in the Gazi Yaşargil Training and Research Hospital between January 2016 and January 2021 were retrospectively scanned using the software system of the hospital. 23 cases who clinically showed symptoms of sepsis and who started empirical antibiotic treat-

ment or whose antibiotic regimen was changed according to the isolated bacterial agent were included in the study. Sepsis was diagnosed according to the American Burn Association (ABA) criteria [7]: presence, in at least one of the initial five days, of clinical suspicion of infection coupled with at least three of the following findings: temperature >39°C or <36.5°C, tachycardia >110 beats/min, tachypnea >25 breaths/min or minute ventilation >12 L/min, thrombocytopenia <100,000/mL, hyperglycemia (untreated plasma glucose >200 mg/dL or intravenous glucose requirement >7 U/h over 24 h), and enteral feeding intolerance (abdominal distension or gastric residuals more than two times feeding rate or diarrhea >2500 mL).

Cases with sepsis, (+) burn wound culture, and blood culture were selected whose WBC, CRP, and PCT results were obtained and studied simultaneously. The first day of symptom manifestation was considered to be a new onset of sepsis. Clinical variables and venous blood samples for WBC, CRP, and PCT determination were collected at admission and every 48 h thereafter until clinical improvement and ICU discharge. The study was conducted with the data obtained entirely through the laboratory software system, In keeping with the Declaration of Helsinki.

Inclusion criteria

1. Patients who hospitalized in the burn care unit due to burn trauma; 2. Patients who had burn area >20% total body surface area; 3. Patients who had burn grade of II-III; 4. Patients diagnosed with sepsis according to the criteria of the American Burn Association.

Exclusion criteria

1. Patients who are not hospitalized in the burn care unit for more than 1 day; 2. Patients who are on the 1st day of their admission to the burn care unit; 3. Patients who had an operation on the day of blood culture and PCT examination or within the next 3 days; 4. Cases with microbiologically suspected contamination in their cultures and those with yeast growth in the culture were excluded from the study.

WBC, CRP and PCT measurements

Serum PCT levels were measured on a Cobas e411 (Roche Diagnostics, Mannheim, Germany) analyser and a CRPLX kit (Roche Diagnostics, Mannheim, Germany) with the electrochemiluminescence immunoassay method using an Elecsys BRAHMS PCT kit (Roche Diagnostics, Mannheim, Germany). Serum CRP levels measured on a Cobas c501 (Roche Diagnostics, Mannheim, Germany) analyser via an immunoturbidimetric method based on latex agglutination were obtained from the laboratory software system and recorded.

The patients' blood PCT and CRP levels, WBC counts, thrombocyte counts, blood cultures and clinical parameters, such as fever, pulse and respiratory counts, were examined. Every other day, the patients were subjected to blood hemogram and biochemistry tests. PCT values were checked on the first and last working days of the week. Blood culture was repeated in patients who had recurrent fever (>38.3°C) despite clinical empirical antibiotic therapy. Due to the suspicion of bacteraemia and bacterial sepsis, samples were taken during blood culture for the determination of blood PCT and CRP levels.

Blood culture

Aerobic and anaerobic blood culture bottles taken during the febrile periods of the patients were loaded into the BACTEC FX (BD Diagnostics, New Jersey, USA) blood culture device. From blood culture bottles that showed positive growths, samples were inoculated on MacConkey agar, sheep blood agar and chocolate agar. After 24 h of incubation at 35-37°C, the plates were evaluated. A Phoenix (BD Diagnostics, New Jersey, USA) automated microbiology system was used for the identification of the isolated bacteria and their antibiotic sensitivities.

Statistical analysis

The CRP and PCT levels in patients with burn wound culture results were expressed as median (25th to 75th percentile) values, given that both variables did not show normal distribution. We performed a non-parametric Mann-Whitney U test in SPSS 17.0 (Statistical Package for the Social Sciences Inc.; Chicago, IL, USA), to determine differences between the two groups. Correlation between CRP and PCT levels was evaluated by a Spearman test. Results with $P<0.05$ for all tests were considered statistically significant.

Table 1. General information of the patients

		number	percent
sex	men	18	78.3%
	women	5	21.7%
age		10.61±17.273 years	
Residential area	rural	17	73.9
	urban	6	26.1
Etiology of burn	flame burn	7	30.4
	electric burn	3	13.0
	scalding	13	56.6
Area of burn	Head neck	5	21.7
	Right upper limb	10	43.5
	Left upper limb	8	34.8
	Front chest + abdomen	14	60.9
	Chest back + back	7	30.4
	perineum	8	34.8
	Right lower limb	14	60.9
	Left lower extremity	16	69.6
Total burn surface area		20.0±12.39 (min: 3-max: 50)	
Burn degree		2.78±0.42 (min: 2-max: 3)	
Late Application Period		4.92±4.23 days (min: 1-max: 16)	
Lenght of hospital stay		11.26±7.17 days (min: 5-max: 36)	

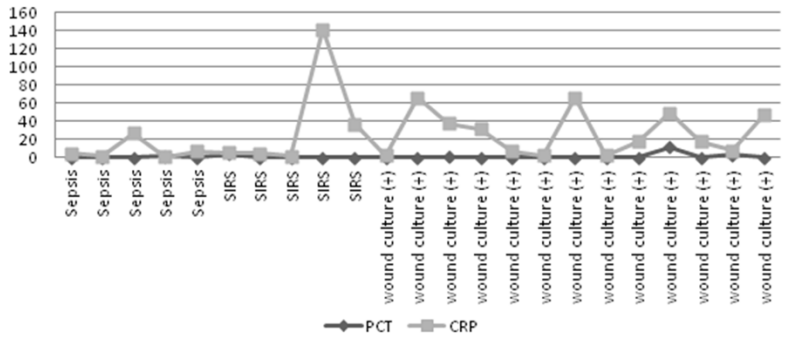

Figure 1. Comparison of PCR and PCT levels in patients.

Results

Of the 23 patients treated in the Gazi Yaşargil Training and Research Hospital burn intensive care unit, 18 (78.3%) were male, and 5 (21.7%) were female. The majority of our patients were male and lived in rural areas (**Table 1**).

The patients applied to our outpatient clinic with a delay of 4.92±4.23 days (min: 1, max: 16). The patients mostly applied to our outpatient clinic during winter, with a rate of 39.1%.

In patients with culture-positive and negative, SIRS, septic and nonseptic patients, WBC, CRP, and PCT results did not statistically different (**Figure 1**).

The wound culture results of the 23 patients were (+), mostly due to *Staphylococcus aureus* in 21.7% (n=5) and *Staphylococcus epidermidis* in 21.7% (n=5) (**Table 2**). Five of the 23 patients with (+) wound culture results had septic findings. The ESBL (+) rate was 25%, and the resistance rate to methicillin was 26.8% in the patients with septic findings. Five patients had sepsis and (+) blood culture results.

Blood levels of WBC, PCT and CRP were increased in all patients. No statistically significant difference was found between the rate of increase in WBC, PCT and CRP values in all patients with (+) wound culture (P=0.613, P=0.544 and P=0.762, respectively). No statistically significant difference was found between the rates of increase in WBC, PCT and CRP values in patients with (+) blood culture results (P=0.536, P=0.600 and P=0.187, respectively) (**Table 3**).

Table 2. Wound site and blood culture results

Wound culture		Number	Percent
pathogens	Staphylococcus aureus	5	21.7
	Staphylococcus epidermidis	5	21.7
	Staphylococcus Haemolyticus	1	4.3
	Pseudomonas aeruginosa	3	13.0
	Pseudomonas putida	1	4.3
	E.Coli	4	17.4
	enterococcus	1	4.3
	klebsiella pneumoniae	1	4.3
	Lactococcus garvieae	1	4.3
	proteus	1	4.3
Blood culture		5	21.7
pathogens	E.Coli	1	4.3
	Klebsiella pneumoniae	1	4.3
	Staphylococcus epidermidis	1	4.3
	Staphylococcus Haemolyticus	1	4.3
	Staphylococcus hominis	1	4.3

Table 3. WBC, CRP and PCT results in SIRS and septic patients

		NUMBER	MIN.	MAX.	MEAN	STD. DEVIATION	*P* VALUE
SEPSIS	PCT	5	0.14	1.88	0.6620	.71100	0.600
	CRP	5	1.0	27.0	8.400	10.6677	0.187
	WBC	5	9.0	37.0	11.0815	4.9558	0.536
TOTAL	PCT	23	0.04	12.16	1.2296	2.65059	0.544
	CRP	23	1.0	141.0	25.739	32.7237	0.762
	WBC	23	6.0	37.0	16.435	8.5802	0.613

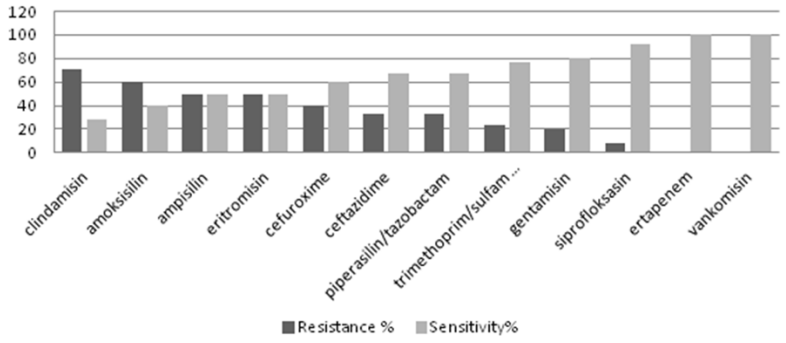

Figure 2. Antibiotic susceptibility of the bacteria resulting from culture.

In the patients with (+) wound culture, the bacteria were most resistant to clindamycin, amoxicillin and ampicillin and most sensitive to ciprofloxacin, ertapenem and vancomycin (**Figure 2**).

Discussion

WBC and CRP results from routinely taken blood samples in burn injuries are constantly high and remain constantly high during hospitalisation in intensive care units. Changes in WBC counts and CRP are not always reliable. When the diagnosis of sepsis is unclear or until the blood bacteriological culture result is obtained, evaluating complete blood count, blood lactate level, CRP and PCT count is recommended [8]. In the treatment and follow-up of patients with burns, Kim et al. demonstrated a benefit from the prognostic feature of PCT [9]. In our clinic, we used complete blood count, CRP and PCT in the laboratory follow-up of infections. We followed the success of antibiotic therapy in patients by looking at WBC, CRP, and PCT levels. In this way, we reduced antibiotic overuse.

Gabay et al. [10] listed many reasons that increase CRP levels (surgery, transfusion, infection) and stated that CRP is not specific as a laboratory biomarker for sepsis pre-diagnosis. Similarly, serum CRP increases have been reported in the clinical condition causing SIRS in patients with burns [11, 12]. We found that CRP elevation was not statistically associated with infection in patients with (+) wound culture (P=0.762) and septic burns (P=0.187). We observed that there was no correlation between patient clinical status and CRP levels. Therefore, despite the continued role of CRP as a biomarker of inflammation in critically ill patients, the lack of certainty as a marker for sepsis, has led to the study of new laboratory biomarkers, such as PCT.

In general, clinical studies have been conducted in patients with burn trauma on the assump-

tion that PCT levels are always elevated as a result of the inflammatory systemic response in sepsis [13]. However, several studies have not shown PCT statistics consistent with infection in patients with burns based on the presence or absence of systemic infection [14-16]. Three recent studies highlighted that serum PCT is a useful biomarker for the early diagnosis of sepsis that develops after burn injuries [17-19]. In our study, the PCT result was high in those with (+) wound culture results (P=0.544) and those with a diagnosis of sepsis (P= 0.600), although no statistically significant difference among septic and nonseptic patients was found. We attribute the increase of PCT to the systemic reactive immune responses in large burn areas. We observed that the PCT value remained consistently high in patients who developed sepsis after burn trauma.

Cabral et al. showed that sepsis diagnosis and clinical follow-up that develops after burn trauma, PCT levels together with blood cultures can help confirm or exclude sepsis in patients [20, 21]. In our study, we found no significant relationship between PCT and blood culture results, and PCT increased in all nonseptic and septic burn trauma patients.

Tunçbilek et al. stated that PCT concentration is more valuable than CRP in predicting the severity of infection [22]. In this study, we found that neither PTC nor CRP were valuable in showing the severity of infection.

According to Analay et al., PCT level can provide information to clinicians for the differentiation of systemic inflammation and sepsis in patients who are clinically suspected of infection and are planned to initiate antibiotics until culture results are available. In addition, the response of an infection to treatment and antibiotic use can be followed by the PCT level together with clinical findings and blood cultures [23]. In our burn intensive care clinic, wound sites and blood and urine cultures of patients with septic symptoms were taken, and then broad spectrum antibiotics were started. The patients were followed up by clinical course and measurement of blood WBC, PCT and CRP levels until culture results were obtained. We observed, level of blood WBC, PCT, and CRP levels returned to initial values with clinical improvement.

In this study, it was observed that CRP, PCT and WBC markers increased with signs of infection and decreased with appropriate treatment in hospitalized patients with the diagnosis of various bacterial infections. However, WBC, CRP and PCT concentrations in septic patients were not significantly higher than those in non-septic patients.

Conclusion

Statistically the laboratory biomarkers WBC, CRP and PCT do not have a superior value in determining and monitoring infection processes in patients with severe burns. However, the study was only a single-center retrospective study and had some limitations. Thus, the conclusion of the study needs to be further studied with a larger sample size and at different treatment centers.

Disclosure of conflict of interest

None.

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