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Differences in the effectiveness of serum biomarkers for the diagnosis of bacterial infections in adult and elderly patients admitted to the emergency department

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Background/aim: This study aimed to evaluate the superiority of procalcitonin (PCT), C-reactive protein (CRP) levels, white blood cell (WBC) counts, and erythrocyte sedimentation rate (ESR) in discriminating among infection, systemic inflammatory response syndrome (SIRS), and sepsis, and their differences according to age groups.

Materials and methods: The patients were divided into an adult group and a geriatric group (over 65 years) and classified according to the presence of infection, SIRS, and sepsis. The patients' laboratory values (PCT, CRP, WBC, ESR), demographic characteristics, and vital signs were taken into consideration.

Results: When the laboratory parameters were evaluated, there were no significant differences in the PCT, WBC, and ESR values between the age groups ($P > 0.05$). CRP was significantly higher in the adult patient group compared to the geriatric group ($P < 0.001$). When the two groups were compared in terms of infection, there were no significant differences in the PCT levels and the WBC count ($P > 0.05$) in SIRS and sepsis. In addition, the CRP levels and the ESR were significantly higher in the adult sepsis patients when compared with the geriatric patients ($P < 0.001$).

Conclusion: PCT levels do not distinguish among infection, SIRS, and sepsis in adult and geriatric age groups.

Key words: Bacterial infections, emergency department, serum biomarkers, adults, geriatrics

1. Introduction

Strikingly, the majority of patients presenting to the emergency department today for nontraumatic reasons are of geriatric age. Advanced age and comorbid chronic disease increase the susceptibility to infection in these patients. It is sometimes difficult to distinguish infectious and noninfectious causes of disease in individuals of advanced age who have related changes in cognition and nonspecific signs of infection. Bacteria cause localized infections by settling on the lungs, kidneys, skin, and soft tissues, depending on their site of entry into the body and their virulence. Localized infection can become systemic due to the host immune response and delays in treatment. The first sign of systemic infection is systemic inflammatory response syndrome (SIRS). The presence of SIRS, along with infection, is defined as sepsis, and delays in antibiotic treatment may increase mortality in these patients (1,2). The evaluation of clinical and laboratory parameters leading to proper treatment planning is an important issue (3). A definitive diagnosis of patients admitted with a suspected bacterial infection can only be made by isolating the bacteria in culture. Culture results are not available for at least 24 h (4). Thus, to demonstrate the presence of bacterial infection in the emergency room, markers are needed that can be determined in serum at an early stage and that can be measured quickly and easily, with high sensitivity (5).

Serum markers, such as C-reactive protein (CRP) levels, white blood cell (WBC) counts, and erythrocyte sedimentation rate (ESR), can be used in the differential diagnosis of bacterial infection. CRP, which is a globulin-structured protein synthesized in the liver, has high sensitivity (6–9).

Procalcitonin (PCT) is an acute-phase reactant protein used in the differential diagnosis of bacterial infections (10). The facts that this marker can be measured in a very short time in serum and that it is an inexpensive test have increased its usability. Many studies have shown that PCT is a superior biomarker in separating infectious and noninfectious causes of disease in patients with signs of infection (11–14).

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In the present study, we aimed to evaluate the superiority of PCT levels, CRP levels, WBC counts, and ESR retrospectively in diagnosing bacterial infections and predicting the prognosis in patients admitted to the emergency department for different reasons.

2. Materials and methods

2.1. Patients and clinical outcomes

We performed a retrospective single-center study at the Ondokuz Mayıs University School of Medicine's Emergency Department. Written approval for the study was obtained from the ethics committee of the Ondokuz Mayıs University School of Medicine. Data were obtained by examining the files of 129 patients who were admitted with a fever (>38 °C) between 2010 and 2012. The patients were divided into an adult age group (18–65 years) and a geriatric age group (over 65 years). Their demographic characteristics, laboratory findings, vital signs (body temperature, systolic and diastolic blood pressure, Glasgow Coma Scale score, respiratory rate, heart rate, and oxygen saturation), concomitant diseases, and past diagnoses were evaluated.

2.2. Definitions

Infection: Presence of microorganisms, invasion of microorganisms of normally sterile host tissue, or an inflammatory response developing as a result of invasion (15).

SIRS: This systemic response was manifested by 2 or more of the following conditions: (a) temperature of >38 °C or <36 °C, (b) heart rate of >90 beats/min, (c) respiratory rate of >20 breaths/min or $PaCO_2$ of <32 mmHg, (d) WBC count of >12,000 cells/mm^3, <4000 cells/mm^3, or >10% immature forms of WBC (16).

Sepsis: Clinical evidence of infection, together with evidence of a systemic inflammatory response to the infection.

2.3. Biochemical analysis

A full blood count and ESR, PCT, CRP, and biochemical measurements were obtained from a blood sample taken in the first 24 h after admission to the hospital.

2.3.1. PCT working method

PCT levels were determined with an enzyme-linked immunosorbent assay (ELISA) using an autoanalyzer (Cobas 5601, Roche, Switzerland). The results were given in ng/mL.

2.3.2. CRP working method

The CRP levels were determined with the nephelometric method using an autoanalyzer (BN II, Marburg, Germany). The results were given in mg/L.

2.4. Statistical analysis

SPSS 15.0 was used to evaluate the data. The Shapiro–Wilk test was used to test the normal distribution of the data. Kruskal–Wallis and Mann–Whitney U tests were used in the analysis of the data that did not fit a normal distribution, and an independent sample t-test was used for analysis of normally distributed data. $P > 0.05$ was considered significant.

3. Results

In this study, 65 (50.3%) of the 129 patients were geriatric and 64 (49.7%) were adults. There was no significant difference in the demographic characteristics between the 2 groups ($P > 0.05$; Table 1). Thirty-four (26.4%) patients were diagnosed with SIRS, 17 (13.2%) with infection, and 78 (60.5%) with sepsis. Among the patients with SIRS, 23 (65.7%) were adults and 12 (34.3%) were geriatric. Five (29.4%) patients diagnosed with infection were adults and 12 (70.6%) were geriatric. Among the patients diagnosed with sepsis, 36 (46.8%) were adults and 41 (53.2%) were geriatric.

There was no significant difference between the 2 groups when their vital signs and demographic characteristics were evaluated ($P > 0.05$). There was also no significant difference in PCT, WBC, or ESR values between the age groups according to their laboratory parameters ($P > 0.05$). The CRP values were significantly higher in the adult patient group compared to the geriatric group ($P < 0.001$) (Table 1).

There was no significant difference in the PCT and WBC values ($P > 0.05$) of either group with regard to infection, SIRS, and sepsis. However, the CRP value was significantly higher in adults diagnosed with sepsis than in adults diagnosed with SIRS or infection ($P < 0.001$). In addition, the CRP value and the ESR were significantly higher in adult sepsis patients when compared with geriatric sepsis patients ($P < 0.001$, $P = 0.015$, respectively) (Table 2).

4. Discussion

In this study, serum PCT was not a suitable marker in the differential diagnosis of infection, SIRS, and sepsis in patients presenting with suspected bacterial infection who were admitted to the emergency department. Serum CRP levels may be a more valuable marker than the other parameters studied to determine the severity of the infection. However, the sensitivity of CRP levels as a marker decreased with advancing age.

The emergency department is responsible for the treatment planning of patients and for directing them to the appropriate section. The basic approach in the presence of bacterial infection is to differentiate noninfectious causes, which can present a similar clinical picture, from infectious causes and initiate appropriate antibiotic therapy. Limiting infection in the tissues with antibiotics may prevent dissemination of bacteria. If infection control

Table 1. Comparison of demographic and laboratory features of the patients.

	Nongeriatric patients n = 64 Mean ± SD/median (IR)/n, %	Geriatric patients n = 65 Mean ± SD/median (IR)/n, %	P-value
Sex (male)	35 (54.7)	40 (61.5)	0.478
GCS	15 (7–15)	15 (3–15)	0.027
Vital signs			
Temperature (°C)	37.39 ± 0.76	37.44 ± 1.02	0.734
RR (breaths/min)	21 (15–38)	22 (12–40)	0.090
HR (beats/min)	96.88 ± 19.23	93.18 ± 18.35	0.267
Oxygen saturation (%)	95.5 (50–99.9)	93.4 (60.9–99.9)	0.338
SBP (mmHg)	104 (80–160)	110 (50–180)	0.497
DBP (mmHg)	70 (40–110)	70 (30–100)	0.986
Laboratory findings			
WBC ($\times 10^6$/L)	7.13 (0.09–31.59)	7.77 (0.19–61.97)	0.526
PCT (μg/L)	0.36 (0.05–44.52)	0.4 (0.05–107.59)	0.400
CRP (mg/L)	126.0 (10.90–539.40)	67.20 (3.41–241.20)	<0.001
ESR (mm/h)	75.22 ± 39.22	58.54 ± 33.92	0.098

SD: Standard deviation, IR: interquartile range, GCS: Glasgow Coma Scale, RR: respiratory rate, HR: heart rate, SBP: systolic blood pressure, DBP: diastolic blood pressure, WBC: white blood cell, PCT: procalcitonin, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate.

Table 2. Evaluation of laboratory values according to the patients age groups and severity of infection.

Parameters	Adult patients				Geriatric patients			
	SIRS	Sepsis	Infection	P-value	SIRS	Sepsis	Infection	P-value
WBC ($\times 10^6$/L)	1.89 (0.09–31.59)	9.60 (0.13–21.55)	8.30 (5.84–25.91)	0.079	2.5 (0.31–61.97)	8.11 (0.19–45.20)	8.78 (5.90–12.31)	0.320
PCT (μg/L)	0.28 (0.05–8.14)	0.42 (0.05–44.52)	1.09 (0.21–4.41)	0.733	0.50 (0.05–26.81)	0.42 (0.05–107.59)	0.35 (0.06–4.17)	0.558
CRP (mg/L)	110.0 $^{ß,\gamma}$ (10.90–180.0)	232.0 $^{*,ß,\&}$ (12.1–539.4)	28.7 $^{\gamma,\&}$ (12.0–52.5)	<0.001	105.0 ‡ (3.41–190.0)	71.9 $^{*,\$}$ (11.0–241.2)	31.35 $^{‡,\$}$ (3.87–85.60)	0.020
ESR (mm/h)	100.0 (8.0–138.0)	87.5 ** (15.0–140.0)	49.0 (13.0–76.0)	0.274	140.0 (140.0–140.0)	49.5 ** (7.0–142.0)	72.0 (20.0–99.0)	0.205

All values are expressed as median (interquartile range). WBC: White blood cell, PCT: procalcitonin, CRP: C-reactive protein, ESR: erythrocyte sedimentation rate, SIRS: systemic inflammatory response syndrome.
*, P < 0.001, compared between groups.
**, P = 0.015, compared between groups.
^{ß}, P < 0.001, compared between groups.
$^{\gamma}$, P < 0.001, compared between groups.
$^{\&}$, P < 0.001, compared between groups.
‡, P < 0.01, compared between groups.
$^{\$}$, P < 0.05, compared between groups.

cannot be achieved in the presence of SIRS signs, sepsis and high mortality may occur. Therefore, identification of the nature of the bacterial infection (infectious or noninfectious cause) is very important, particularly in the emergency room, which is the first treatment center for such patients.

The inflammatory process starts in sepsis by activation of the innate immune response in an uncontrolled manner and the release of cytokines, such as tumor necrosis factor-α, interleukin-1, interleukin-6, interleukin-8, and interferon-γ, from macrophages and endothelial and epithelial cells in response to antigenic bacterial products (17,18). In a normal inflammatory response, these cytokines are limited to the site of local infection. However, if they diffuse into the circulation by excessive synthesis, they can cause serious endothelial cell damage. Endothelial injury may cause hemodynamic changes and organ failure. Thus, the severity of the host's immune response to infection is the most important factor affecting the course of the infection in sepsis (19). Classic signs of sepsis may not be detected in elderly and immunosuppressed patients because their inflammatory response decreases (20).

A number of studies have investigated clinical and laboratory markers, including PCT, CRP, and other proinflammatory cytokines, that may be helpful in the differential diagnosis and prognosis of bacterial infections in the elderly (7,12,21–23). A recent study that investigated the diagnostic value of PCT, IL-6, and CRP in 539 patients with suspected infection who were admitted to the emergency department found that PCT was superior (11). Magrini et al. reported that PCT increased in nonsurvivors during treatment but significantly decreased in survivors in patients admitted to the emergency department with signs of infection (12). Infection, combined with other diseases, worsens the prognosis and increases the mortality of many patients admitted to the emergency department. Therefore, the detection of bacteremia in patients can prevent such mortality. Cornelissen et al. evaluated the relationships between PCT, WBC, and CRP values and mortality and complications in patients with infective endocarditis admitted to the emergency department (24). They found that PCT (cut-off value: >0.5 ng/mL) was more valuable in predicting poor results. In another study, PCT was superior to CRP and WBC in distinguishing bacteremic and nonbacteremic patients who were followed due to acute pyelonephritis, and in these patients PCT reduced the need for blood cultures in diagnosis (25). In this study, there was no significant difference between the PCT, WBC, and ESR serum levels of the adult and geriatric patients with infection, SIRS, or sepsis. However, CRP was significantly higher in the adult patient group with sepsis compared to adult patients with infection and SIRS. Unlike other studies, we did not find that PCT was successful in differentiating infection, SIRS, and sepsis. This may be due to the absence of measurements other than the initial laboratory values of the patients upon admission to the emergency department. The high CRP value in sepsis was an expected outcome. However, the fact that it was higher in adult patients with sepsis than in geriatric patients with sepsis was remarkable. We attribute this finding to the elevated acute-phase reactions of adult patients who have a more active immune system (20). Comprehensive studies investigating the role of CRP in the follow-up and diagnosis of infection in geriatric patients would help to clarify this issue.

There were some limitations in our study. First, it was not possible to obtain all the required laboratory data in this retrospective study. Therefore, only patients admitted to the emergency room with fever and single PCT, CRP, WBC, and ESR values measured in the first 24 h were included in the study. PCT and CRP values in the subsequent 24–48 h were unavailable. As noted earlier, due to the pharmacokinetics of PCT and CRP, different results could be obtained by repeated measurements, as found by several other researchers (22,24). The second limitation concerns patient acceptance criteria. PCT is quickly synthesized by status organs such as the liver and serum levels could have decreased in patients with infections and liver disease, so they may have been excluded from the study. Third, in the presence of bacterial infection, serum PCT levels, which may be indicative of a rapid response to antibiotic treatment, decrease. Therefore, patients with a history of antibiotic use who presented to the emergency department were excluded from the study.

In summary, there was no significant difference in the ability of PCT to distinguish among SIRS, infection, and sepsis in either adult or geriatric age groups in the emergency department. CRP was successful in differentiating infection and sepsis according to the data obtained in this study. Repeated measurements of serum markers are needed to aid the identification of infectious versus noninfectious causes of patient symptoms. The sensitivity of CRP decreased with age. This important finding requires further research.

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