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Original Article

C-reactive protein in view of prognosis in sepsis

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Abstract

Introduction

Sepsis is the host reaction to invading microbes. The septic response generally occurs when immune defenses fail to contain an invading microbe and may also be induced by microbial exotoxins. C-reactive protein (CRP) is an acute-phase protein in humans and an important component of the innate immune system. CRP activates complement's classical route, which is one of its key strategies for defending the host.

Patients and methods

This study was conducted on 20 patients with systemic sepsis and admitted to the critical care unit; moreover, 20 healthy participants were studied as a control group.

Results

Both groups were matched for age and sex, with 55% male and a mean age of 43.5 years in the group with systemic sepsis. Regarding the outcome of patients, 45% were survivors. Regarding the description of patients, 55% were surgical and 45% were nonsurgical types among septic patients. We found a highly significant difference in CRP between the two groups regarding CRP. We found no significant difference in CRP levels between septic shock and nonseptic shock. CRP level was consistently higher in nonsurvivors. CRP levels showed no significant difference on days 1 and 7 in surviving patients, but the levels increased significantly from 1 to 7 days in nonsurvivors. We found no significant difference in the length of stay between patients with high CRP levels and those with low CRP.

Conclusion

CRP is an acute-phase protein whose concentration increases in association with bacterial infection, inflammation, or tissue necrosis. CRP is most useful in that it shows the greatest and most rapid increase, up to a thousand-fold over the baseline level. A persistent elevation in CRP indicates increased continuation of the pathologic process or a postoperative complication in the case of a surgical patient.

Keywords: Critical care, C-reactive protein, sepsis

Introduction

Sepsis is the host's response to invading microorganisms, and it is characterized by a rapidly amplifying polyphony of signals and responses that may spread beyond the invaded tissue. Fever or hypothermia, tachypnea, and tachycardia are frequently associated with the development of sepsis, the systemic reaction to microbial infection. When counter-regulatory control mechanisms are overloaded, homeostasis may collapse and serious organ dysfunction may occur (severe sepsis); additional regulatory imbalance results in septic shock, which is characterized by hypotension in addition to organ dysfunction. The risk of death rises dramatically when sepsis develops to septic shock [1].

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Sepsis is typically recoverable, whereas septic shock frequently results in death despite standard therapy. The septic reaction is frequently activated when bacteria spread from the gastrointestinal system or skin into adjacent tissues, and infection of a single tissue may result in bacteremia or fungemia. Alternatively, microbes can be injected directly into the bloodstream (through intravenous catheters, for example). The septic reaction generally occurs when the immune system

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fails to contain an invading pathogen. Owing to the fact that the majority of cases are caused by microorganisms that do not normally cause systemic disease in healthy hosts, impairments in nonadaptive host components may be the most relevant reason. Exotoxins produced by microorganisms, which act as superantigens, can also initiate a septic reaction.

C-reactive protein (CRP) was first reported by Tillett and Francis [2] and was originally termed for its ability to bind streptococcus pneumonia's C polysaccharide. CRP is a 115.000-D cyclic pentameric protein composed of five protomers containing 206 amino acids each. Its sequence is largely utilized, and there is just one polymorphism known [3,4], but no deficient state has been described [5,6]. CRP is an acute-phase protein that plays a critical role in the innate immune system in humans. CRP activates the complement's classical pathway, which is one of its primary defense mechanisms. CRP interacts with immune system cells via FC gamma receptors, implying that it may operate as a bridge between innate and adaptive immunity, providing an early, effective antibacterial response [7,8].

Furthermore, it may protect against the deadly adverse effects of bacterial products by preventing the harmful inflammatory response to lipopolysaccharide and cytokines. The discovery of CRP's interaction with FC gamma receptors has led to a better understanding of CRP's role in both the innate and immune systems. CRP has been shown in several trials to be effective in diagnosing and/or follow-up of infections in specific conditions such as urinary tract infection, community-acquired pneumonia, and infective endocarditis [9,10].

Aim

The aim was to assess CRP as a model for diagnosis and follow-up of infection and prognostic marker for sepsis.

Patients and methods

The patients were recruited from a 15-bed medical ICU admitting patients from all the departments and from ICUs of other hospitals.

Inclusion criteria

A total of 20 patients were admitted with systemic sepsis as indicated by the following:

(1) Presence of a known site of infection indicated by positive blood culture or by radiography or physical examination evidence of an infective collection.
(2) Evidence of a systemic inflammatory response indicated by at least two of the following:
    (a) Fever or hypothermia.
    (b) Tachypnea (>20 breaths per minute) or need for mechanical ventilation.
    (c) Tachycardia (heart rate 90 beats per minute).
(3) White blood cell counts of 12 000 cells/mm^3 or 4000 cells/mm^3.

In addition, they should have stayed in the ICU for more than 24 h.

A total of 20 controls (no criteria of systemic sepsis) were also included.

Exclusion criteria

The following were the exclusion criteria:

(1) Patients for whom data collection was insufficient.
(2) Patients who refused to participate in the study.

Patients included in the study were subjected to the following:

(1) Clinical evaluation: clinical history, full clinical examination, ECG, echo, and radiograph.
(2) General laboratory investigations: liver and kidney functions, complete blood picture, blood gases, urine, endotracheal cultures, urine analysis, and Na and K levels.
(3) Specific laboratory investigations: CRP is one of a group of proteins known as 'acute-phase proteins,' whose concentration increases in association with the presence of bacterial infection, inflammation, or tissue necrosis. CRP is most useful in that it shows the greatest and most rapid increase, up to a thousand-fold over the baseline level. The rise in CRP is exponential, with a doubling time of 8 h. Peak levels are usually reached in about 72 h, returning to baseline in 4–6 h if healing proceeds normally. A persistent elevation in CRP indicates the continuation of the pathologic processor, a postoperative complication in the case of a surgical patient.

Ethical considerations

The study was approved by the institutional Ethics Committee of National Heart Institute no. HNI-00075.

Statistical methods

Mean and SD were used to express all continuous data. Frequency tables were used for categorical data. Unpaired *t* test after checking normality was performed for all continuous data for comparison of two independent groups. χ^2 test was used for all qualitative data. Paired *t* test was used for paired comparison of all continuous data. Multivariate discrimination analysis and then a stepwise approach to select the best independent predictors for diagnosing systemic sepsis were done. *P* values of 0.05 or less were considered statistically significant. All tests were performed using SPSS program, version 10 (SPSS Inc. (1999). SPSS Base for Windows. SPSS Inc., Chicago, IL).

Results

This study was conducted on 20 patients with systemic sepsis and admitted to the Critical Care Department. A total of 29 healthy participants were studied as controls, and both groups were matched for age and sex, as shown in Tables 1 and 2, respectively.

Our study included 20 patients, comprising 11 (55%) males and nine (45%) females, with a mean age of 34.6 years (range, 18–51 years). The control group included 20 patients, comprising 12 (60%) males and eight (40%) females, with a mean age of 43.5 years (range, 30–56 years) (Tables 1 and 2).

The outcome of patients

Data show that out of the studied patients with systemic sepsis, nine (45%) were survivors and 11 (55%) were nonsurvivors (Table 3).

Description of patients

Septic patients were classified into surgical and non-surgical (medical) types. A total of 11 (55%) patients were surgical and nine (45%) patients were nonsurgical (Table 4).

Table 1: Age of patient and control groups

Parameters	Group	*n*	Mean±SD	*P*
Age	Patients	20	34.6±16.5	0.063
	Control	20	43.5±12.6	

Table 2: Sex of patient and control groups

Sex	Male [*n* (%)]	Female [*n* (%)]	Total [*n* (%)]
Patients	11 (55)	9 (45)	20 (100)
Control	12 (60)	8 (40)	20 (100)
P		0.749	

Table 3: Outcome of patients

Outcome	Frequency	Percent
Survivors	9	45
Nonsurvivors	11	55

Table 4: Frequency of surgical and nonsurgical patients

Type	Frequency	Percent
Surgical	11	55
Nonsurgical	9	45

Table 5: Mean C-reactive protein levels on admission in patient and control groups

Parameters	Groups	Number of patients	Mean±SD	*P*
CRP on admission	Patients	20	16.82±3.76	0.0001
	Control	20	0.45±0.1	

CRP, C-reactive protein.

Septic marker: C-reactive protein

Comparing the CRP levels of patients with those of control, we found a highly significant difference in the CRP levels between the two groups, where patients had a mean CRP level of 16.8 ± 3.8 mg/dl and the controls had a mean CRP level of 0.45 ± 0.1 mg/dl, with *P* value of 0.0001 (Table 5).

CRP levels were measured for patients on days 1, 3, 5, and 7. It is obviously seen that CRP levels were significantly higher in patients with more than one organ dysfunction than in those having single organ dysfunction, as mean CRP levels in patients with one organ dysfunction on days 1, 3, 5 and 7 were 8.7, 10.13, 10, and 13.95 mg/dl, respectively, whereas in those with multiorgan dysfunction were 18.7, 30.5, 33.8, and 48.23 mg/dl in days 1, 3, 5, and 7, respectively (Table 6). Data were statistically significant starting from day 3 and up till day 7.

We found no significant difference in CRP levels between patients exhibiting septic shock and those with no septic shock on days 1, 3, 5, and 7.

Patients with septic shock had mean CRP levels of 19.3, 25.96, 30.275, and 41.17 mg/dl on days 1, 3, 5, and 7, respectively, whereas those with no septic shock had mean CRP levels of 10.87, 37.2, 36.67, and 50.58 mg/dl in days 1, 3, 5, and 7, respectively (Table 7).

Our results showed that CRP level was consistently higher in nonsurvivors than in survivors. Data were statistically significant on days 3 and 5, where mean CRP levels were 13.9 and 20.86 mg/dl for survivors, respectively, and 42.98 and 41.64 mg/dl for nonsurvivors, respectively, yet were not statistically significant on days 1 and 4, where mean CRP levels for survivors were 11.9 and 29.8 mg/dl, respectively, and for nonsurvivors were 19.9 and 55.6 mg/dl, respectively (Table 8). This means that patients with higher CRP levels showed higher mortality than those with lower CRP levels all over the study.

We found no significant difference between mean CRP levels on days 1 and 7 in survived patients ($P = 0.19$) (Table 9), whereas in nonsurvivors, the difference was statistically significant where mean CRP level increased significantly from days 1 to 7 ($P = 0.059$), indicating the deterioration of the case and predicting the poor outcome of patients (Table 10).

Table 6: Mean C-reactive protein levels and number of organ dysfunction

Parameters	Groups	*n*	Mean±SD	*P*
CRP level (day 1)	Patients with 1 organ dysfunction	3	8.7±3	0.0725
	Patients with >1 organ dysfunction	15	18.71±18.9	
CRP level (day 3)	Patients with 1 organ dysfunction	3	10.13±5.8	0.018
	Patients with >1 organ dysfunction	15	30.5±27	
CRP level (day 5)	Patients with 1 organ dysfunction	2	10±7.07	0.027
	Patients with >1 organ dysfunction	14	33.8±23.9	
CRP level (day 7)	Patients with 1 organ dysfunction	2	13.95±8.6	0.025
	Patients with >1 organ dysfunction	11	48.23±37.1	

CRP, C-reactive protein.

Table 7: Mean C-reactive protein levels and deterioration of systemic sepsis into septic shock

Parameters	Groups	*n*	Mean±SD	*P*
CRP level (day 1)	Patients with septic shock	13	19.3±20.3	0.174
	Patients without septic shock	7	10.87±4.4	
CRP level (day 3)	Patients with septic shock	13	25.96±24.8	0.434
	Patients without septic shock	7	37.2±±31.5	
CRP level (day 5)	Patients with septic shock	12	30.275±24	0.583
	Patients without septic shock	6	36.67±21.8	
CRP level (day 7)	Patients with septic shock	9	41.17±37.4	0.647
	Patients without septic shock	5	50.58±34.4	

CRP, C-reactive protein.

Table 8: Mean C-reactive protein levels and outcome of patients

Parameters	Groups	*n*	Mean±SD	*P*
CRP level (day 1)	Survivors	9	11.9±10.6	0.277
	Nonsurvivors	11	19.9±20.3	
CRP level (day 3)	Survivors	9	13.9±9.8	0.01
	Nonsurvivors	11	42.98±29.9	
CRP level (day 5)	Survivors	8	20.86±14.2	0.042
	Nonsurvivors	10	41.64±24.8	
CRP level (day 7)	Survivors	6	29.81±38.9	0.211
	Nonsurvivors	8	55.6±30.3	

CRP, C-reactive protein.

Table 9: Mean C-reactive protein levels on days 1 and 7 among survivors

Parameters	*n*	Mean±SD	*P*
CRP (day 1)	6	13.57±13	0.191
CRP (day 7)	6	29.82±39	

CRP, C-reactive protein.

Table 10: Mean C-reactive protein levels on days 1 and 7 among nonsurvivors

Parameters	*n*	Mean±SD	*P*
CRP (day 1)	8	13±4.4	0.059
CRP (day 7)	8	55.6±30.3	

CRP, C-reactive protein.

Table 11: C-reactive protein level and length of hospital stay

Variance	*n*	*r*	*P*
CRP (day 1) and LHS	20	−0.116	0.629
CRP (day 2) and LHS	20	−0.87	0.626
CRP (day 3) and LHS	18	0.142	0.575
CRP (day 4) and LHS	14	0.144	0.622

CRP, C-reactive protein; LHS, length of hospital stay.

Correlating the CRP levels with the length of hospital stay, we found no significant difference in the length of stay between patients with high CRP levels and those with low CRP levels on days 1, 3, 5, and 7 (Table 11).

Discussion

By analyzing the data of systemic septic patients included in our study, we found that the survivors were nine (45%) patients and the nonsurvivors were 11 (55%). Shoemeker *et al*. [11] found mortality of 20–50% in cases of sepsis. The present study showed that survivors had a mean age of 27.67 years, whereas nonsurvivors had a mean age of 40.37 years. Mizock had mentioned in 1984 that elderly septic patients are more liable to mortality than younger septic patients. Bacterial infection is a potent stimulus, leading to rapid elevation of CRP level. Changes in plasma CRP can be useful in diagnosing infection and in the follow-up of the clinical course, with a fall in CPR level indicating resolution of infection [8]. Matson *et al*. [12] found that a 25% or greater increase in the plasma CRP level was highly suggestive of sepsis. Their findings were in agreement with our study, as we found a highly significant difference in the mean CRP level between the patient group (16.82 mg/dl) and the control group (0.45 mg/dl), with *P* value less than 0.0001. So, we can acknowledge that CRP is a useful diagnostic marker of systemic sepsis in the ICU [13]. Their finding agreed with our study, confirming the relation between CRP and multiorgan dysfunction. A study by Peltola and Jaakkola [14] found that mean CRP levels were insignificantly higher in the septic shock group than in the systemic sepsis group. Our study found higher mean CRP levels in patients with septic shock (19 vs. 10 mg/dl in patients with sepsis) on day 1 of admission. Later on, the mean CRP was higher in patients with sepsis without shock; however, the differences were statistically insignificant on days 3, 5, and 7. (25.9, 30.2, and 41.1 mg/dl, respectively, in patients with septic shock vs. 37.2, 36.6, and 50.5 mg/dl, respectively, in patients with no septic shock). Lobo *et al*. [15] concluded that the general CRP level correlates with the outcome, and persistently high levels carry the worst prognosis. Studying the relation between CRP levels on days 1, 3, 5 and 7 and the outcome of patients, we found that mean CRP levels were all over the study higher in nonsurvivors than in survivors, indicating the success of CRP as a prognostic tool guiding us to the outcome of patients with systemic sepsis.

Conclusion

CRP is a useful model for diagnosis and follow-up of infection and a prognostic marker for sepsis.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form, the legal guardian has given her consent for images and other clinical information to be reported in the journal. The guardian understands that her names and initials will not be published and due efforts will be made to conceal the patient's identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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