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Prognostic evaluation for the need of intensive care in cases of severe sepsis by measurement of endotoxin activity and procalcitonin

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Abstract

Objective : It can be difficult to select appropriate intensive care for cases of sepsis admitted to the intensive care unit (ICU). We investigated the relationships between endotoxin activity (EA), procalcitonin (PCT) or Interkeukin-6 (IL-6) levels and severity of illness. We also investigated whether measurement of EA or PCT level of patients admitted to the ICU can predict the need for direct hemoperfusion with a polymyxin B immobilized fiber column (PMX-DHP).

Methods : Thirty-three patients admitted to the ICU with severe sepsis or septic shock were assessed. Within 6 h of admission, blood samples were collected and APACHE II and SOFA scores were determined, and EA, PCT and IL-6 levels were measured. Patients were divided into 3 groups : low (L-group), intermediate (M-group), and high (H-group), based on their EA and PCT levels. We analyzed the relationships between PMX-DHP implementation and EA or PCT level and the relationship between EA levels and causative bacteria.

Results : Although no significant correlation was found between APACHE II or SOFA scores and EA, PCT or IL-6 levels, there was a good correlation between PCT and IL-6 levels. The mean EA level in the gram-negative infection group was 0.58±0.19 vs. 0.45±0.22 for the gram-positive infection group. The rates of PMX-DHP implementation were not significantly different in the 3 EA and PCT groups [38.4% (5/14) EA-L, 20% (1/5) EA-M, 35.7% (5/14) EA-H group, respectively : 0% (0/4) PCT-L, 40% (4/10) PCT-M, 36.8% (7/19) PCT-H group, respectively].

Conclusion : The EA level was not associated with the existence of gram-negative infection and also did not correlate with illness severity. Significant correlation was found between PCT and IL-6 levels, although PCT and IL-6 levels did not correlate with the severity of illness. EA and PCT measurements were not found useful for the implementation of PMX-DHP.

Introduction

The principle of sepsis treatment involves the determination of the infectious focus, selection of the appropriate surgical operation, drainage of the focus, administration of antibiotics for the causative microorganisms, and support for organ failure. Despite the progress made in diagnostic techniques and critical care medicine and development of treatment guidelines, the mortality rate for sepsis is still high (from 20 to 50%). Clearly, the detection of the causative bacteria, fungi, and viruses are useful for therapeutic strategy. However, conventional tests for the detection of the causative microorganisms, including blood culture, are not sensitive enough and are time-consuming. Therefore, clinicians almost always have to start empirical antimicrobial therapy, without the

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determination of the causative microorganisms. The determination of the severity of the disease is also important to start the appropriate treatment as early as possible.

Endotoxin or lipopolysaccharide (LPS) is a major cell wall component of gram-negative bacteria and a potent trigger of innate immunity ; it activates macrophages and neutrophils to produce inflammatory mediators and cytokines in the host. Endotoxin plays a major role in the development of sepsis. In order to diagnose sepsis and start appropriate therapy, it is also important to know whether the infection is caused by gram-negative bacteria or by endotoxin.

Several inflammation markers such as C-reactive protein (CRP) and white blood cell count (WBC) may not be enough to identify critically ill patients who need antimicrobial therapy, because the sensitivity and specificity for bacterial infection are low and sometimes misleading. Procalcitonin (PCT) is a 13-kDa, 116-amino acid polypeptide glycoprotein. As previously reported by Assicot et al., the serum PCT concentrations were elevated in patients with bacterial infection[1]. Further clinical studies have indicated that sepsis related to systemic bacterial infection, but not fungal or viral infection, could induce higher concentrations of serum PCT and that the levels of PCT correlated with the severity of sepsis[2].

According to the recently accepted picture of the pathophysiology of sepsis, excess pro-inflammatory cytokines play a pivotal role in the progression of shock, and organ failure[3]. Among these pro-inflammatory cytokines, the blood level of interleukin (IL)-6 is reported to be a good index of cytokine cascade activation and to be relevant to the severity of illness[4].

Direct hemoperfusion with a polymyxin B immobilized fiber column (PMX-DHP), which could remove circulating endotoxin by adsorption and prevent the progression of the inflammatory cascade of sepsis, has been used for the treatment of severe sepsis or septic shock in Japan since 1994, and its efficacy has been reported in many clinical studies[5-7]. Septic shock induced by gram-negative infection is one of the major causes of multiple organ dysfunction syndrome (MODS) in patients treated in intensive care units (ICU). In the patients who present with shock by gram-negative infection, PMX-DHP should be considered at the appropriate time. Therefore, it is important to recognize the causes of sepsis and determine the severity of the clinical condition as early as possible.

It has been difficult to measure endotoxin reliably in biological fluids. The most widely used method — the chromogenic limulus amebocyte lysate assay (LAL) — has certain limitations with regard to the detection and quantification of endotoxin in plasma or whole blood. Romaschin et al. developed a novel technique — the endotoxin activity assay (EAA) — for detecting endotoxin in whole blood using neutrophil-dependent chemiluminescence on the basis of the ability of antigen-antibody complexes to prime neutrophils and augment respiratory burst response[8]. They reported that the EAA would be a useful diagnostic tool for the investigation of gram-negative infection and incipient sepsis[9]. The aim of this study was to investigate the correlation between the level of severity in septic patients admitted to the ICU, and levels of EA, PCT or IL-6, and to determine whether the measurement of EA or PCT is helpful in predicting the use of PMX-DHP treatment.

Patients and methods

Subjects

From June 2008 to June 2009, we studied 33 patients who developed severe sepsis or septic shock and were admitted to the medical-surgical ICU. Sepsis is defined as infection plus systemic inflammatory response syndrome (SIRS), in accordance with the criteria of the American College of Chest Physicians/Society of Critical Care Medicine Consensus Conference[10]. Severe sepsis is defined as sepsis plus sepsis-induced organ dysfunction or tissue hypoperfusion. Septic shock is defined as sepsis-induced hypotension persisting despite adequate fluid resuscitation. Patient culture samples were collected from all sites suspected to be infectious. Infections were considered to be present if at least one blood culture was positive for pathogenic microorganisms, or if there was clinical evidence of local infection of microorganisms in sterile body fluid or sites, such as ascites, sputum, urine, spinal fluid, or a wound with purulent discharge. Patients were treated according to Surviving Sepsis Campaign Guidelines 2008[11]. The PMX-DHP treatment was performed when a patient still showed mean arterial blood pressure ≤65 mmHg regardless of appropriate fluid resuscitation and the use of catecholamine (dopamine ≥5 μg/kg/min or norepinephrine ≥0.05 μg/kg/min). Other blood purification therapy (including continuous hemodiafiltration or hemodialysis) was performed at the discretion of the responsible physicians because there were no standardized criteria. Within 24 h after ICU admission, comprehensive clinical and laboratory data, endotoxin activity (EA) and PCT levels, and interleukin (IL)-6 were checked. Baseline severity of illness was quantified using the Acute Physiology and Chronic Health Evaluation II (APACHE II) score[12] and Sepsis-related Organ Failure Assessment (SOFA) score[13]. Survival status was assessed 28 days after ICU admission. This study protocol was approved by the ethical committee of Tokyo Medical University, Hachioji Medical Center.

Measurement of EAA

Blood samples were collected for endotoxin assay within 6 h after admission to the ICU and all samples

were assayed within 30 min of collection. Samples were collected in Becton Dickinson sterile Vacutainer® tubes containing EDTA anti-coagulant, through an indwelling arterial catheter. The EAA analyses were performed by laboratory technicians at the clinical laboratory department in our hospital. Serum EA level was measured using Smart Line EAA Luminometers according to the manufacturer's protocol (Spectral Diagnostics, Inc., Toronto, Ont., Canada). All samples for EAA were measured in duplicate and the mean from the duplicates is used for the result of EA level, classified at low (<0.4, L group), intermediate (0.4≤ <0.6, M group), and high (≥0.6, H group), according to the classification of the MEDIC study by Marshall et al[14]. The EA level of 0.4 is approximately equivalent to an endotoxin concentration of 25 to 50 pg/mol, and the level of 0.6 equivalent to 100 to 200 pg/mol of *E. coli* 055 : B5 LPS.

Measurement of PCT

PCT concentrations were measured at the same time of EAA measurement using immune luminometric assay (SphereLight Brahms PCT ; Brahms Diagnostica, Berlin, Germany) and a SphereLight 180 luminometer (Olympus Corporation, Tokyo, Japan), modified as previously described[15]. This assay has an optimized functional sensitivity of 0.06 ng/ml. On the basis of previous studies in Japan[16], PCT concentrations were classified at low (<2 ng/ml, L group), intermediate (2≤ <10 ng/ml, M group), and high (≥10 ng/ml, H group). If the PCT concentration is less than 2 ng/ml, the possibility of severe sepsis is low. If the concentration is between 2 and 10 ng/ml, severe sepsis is suspected, and if the concentration is greater than 10 ng/ml, the risk of progression to severe sepsis or septic shock is high.

Measurement of other markers

The serum IL-6 concentration was determined by enzyme-linked immunosorbent assay (ELISA ; human IL-6 ANALYZA Immunoassay Kit ; TECHNE, Minneapolis, MN, USA). Other conventional markers were tested using commercially available kits and instruments.

Direct hemoperfusion with a polymyxin B immobilized fiber column (PMX-DHP) treatment

A polymyxin B immobilized fiber column (Toraymyxin 20-R ; Toray Industries Inc., Tokyo, Japan) was used for the PMX-DHP treatment. A percutaneous flexible double-lumen catheter for blood access was inserted into the internal jugular vein or the femoral vein, and blood was both drawn from and returned to the vein. Treatment was carried out for 2 h at a flow rate of 80-100 ml/min as previously described[17]. Nafamostat mesilate (Torii Pharmaceuticals Co. Ltd., Tokyo, Japan), a protease inhibitor, was used as the anticoagulant. PMX-DHP was performed in 11 patients who had septic shock (caused by any organisms) and fulfilled the initiation criteria given above.

Statistical Analysis

Data were expressed as means±standard deviation (SD). Categorical variables were presented as proportions and were analyzed by using the χ^2 test or Fisher's exact test, where appropriate. To compare 3 independent groups we used analysis of variance (ANOVA) or the Kruskal-Wallis test (data non-normally distributed) with Bonferroni corrections. A P value of less than 0.05 was considered statistically significant. Statistical calculations were performed with SPSS statistical software (version 17.0 ; SPSS).

Results

Patient Characteristics

During the 1-year study period, 33 patients with a diagnosis of severe sepsis or septic shock were admitted to the medical-surgical ICU. Twenty-three patients met the criteria for septic shock and the remaining 10 patients met the criteria for severe sepsis. Demographic data for these 33 patients are summarized in Table 1. The underlying diseases of the enrolled patients were intra-abdominal cavity infection (15 patients), pneumonia (8 patients), urinary tract infection (3 patients), meningitis (2 patients), soft tissue infection (2 patients), and other infections (3 patients). The causative bacteria were gram-positive bacteria (9 patients), gram-negative bacteria (10 patients), virus (1 patient), and unknown (13 patients). The microbiological findings in patients with severe sepsis or septic shock are presented in Table 2. Blood cultures were performed in all patients, and 13 cultures (39%) were positive for pathogenic microorganisms (gram-positive, *N*=7 ; gram-negative, *N*=6). Ten pa-

Table 1 Demographic characteristics of the patients

Parameter	Mean ± SD or Median (range)
Age, years	72.7±11.3
Gender : male/female	25/8
APACHE II score	25.2±7.7
SOFA score	9.7±3.5
EA	0.50±0.25
PCT (ng/ml)	12.7 (0-200)
CRP (mg/dl)	14.9±9.8
IL-6 (pg/ml)	1,920 (9-1,480,000)
WBC (10^3/mm^3)	10.1±9.1
ICU length of stay, days	10.4±8.0
Mortality, number. (%)	10 (30.3%)

Continuous parameter data are expressed as means±SD. Discontinuous parameter data are expressed as median values (minimum to maximum) ; APACHE, Acute Physiology and Chronic Health Evaluation ; SOFA, Sepsis-related Organ Failure Assessment ; EA, Endotoxin activity ; PCT, Procalcitonin ; CRP : C-reactive protein ; IL-6 : Interleukin-6 ; WBC : White blood cell count ; ICU, intensive care unit

Table 2 Sites and microbiological findings in patients with severe sepsis or septic shock

Sites and isolated organism	No. of patients
Abdomen	
Gram-negative	
Escherihia coli	1
Klebsiella speicies	4
Enterobacter cloacae	1
Gram-positive	
Enterococcus faecalis	1
Unknown	9
Lung	
Gram-negative	
Pseudomonas aeruginosa	1
Escherihia coli	1
Gram-positive	
Streptococcus pneumoniae	2
Fungi	
Asprugillus fumigatus	1
Candida species	1
Unknown	4
Urinary tract	
Gram-negative	
Escherihia coli	3
Bloodstream	
Gram-positive	
Staphylococcus speicies	4
Central nervous system	
Gram-positive	
Streptococcus pneumoniae	1
Virus	1
Skin/soft tissue	
Gram-positive	
Staphylococcus aureus	1

Positive cultures were detected from more than 1 site in 9 patients
Multiple microorganisms were isolated in 9.1% (3/33) of patients

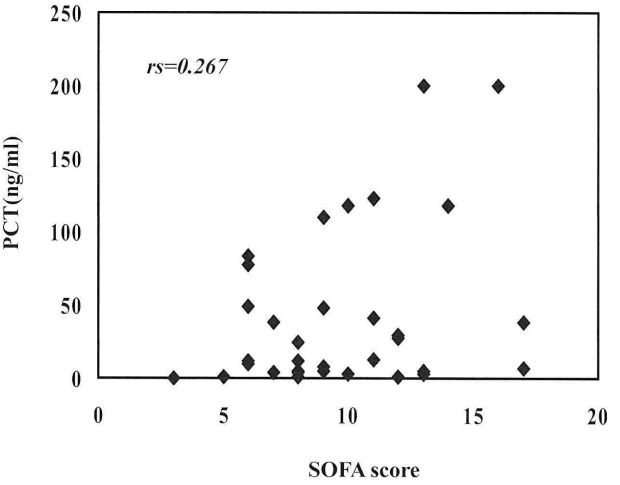

Fig. 1 Correlation of procalciotin (PCT) with SOFA score. A weak correlation was found between PCT and SOFA score, their Spearman's rank correlation coefficient was 0.267. PCT, Procalcitonin ; SOFA, Sepsis-related Organ Failure Assessment

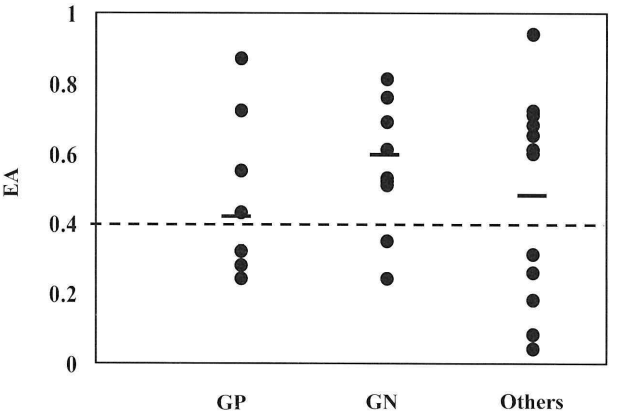

Fig. 2 Relationship of the causative bacteria with endotoxin activity (EA) level. The mean EA level in the gram-positive (GP) infection group was 0.45±0.22 and the mean in the gram-negative (GN) infection group was 0.58±0.19. There was no significant correlation of the causative bacteria with EA level.

tients (30%) died within 28 days.

Correlation of EA, PCT and IL-6 levels with illness severity at the time of admission to ICU

There was no significant correlation of the APACHE II score with EA, PCT or IL-6 level. There was also no significant correlation of SOFA score with EA, PCT or IL-6 level. While the correlation of Pearson's coefficient between EA level and SOFA score was low (r=0.117), the Spearman's rank correlation coefficient between PCT and SOFA score was relatively high (rs=0.267) (Fig. 1). We investigated the relationship between EA and PCT levels. There was also no significant correlation between any EA value group and the PCT, nor any PCT value group and the EA. Their Spearman's rank correlation coefficient was very low (rs=0.078).

Association of EA and PCT levels with both gram-negative and gram-positive infection

Furthermore, we investigated the relationship of the causative bacteria (gram-positive bacteria, gram-negative bacteria, and the others) with EA or PCT level. The mean EA level in the gram-negative infection group was 0.58±0.19, and the mean in the gram-positive infection group was 0.45±0.22 (Fig. 2). The median PCT value in the gram-negative infection group was 43.5 ng/ml, and the median in the gram-positive infection group was 27.3 ng/ml. There was no significant correlation of the causative bacteria with EA or PCT level. These results were not consistent with our expectation that the EA lev-

el should be high for gram-negative bacterial infections. EA levels were ≥0.4 in 8 of 10 patients in the gram-negative infection group. Otherwise, 5 of 9 patients in the gram-positive infection group had EA levels <0.4. EA levels in the gram-negative infection group tended to be higher than those of gram-positive infection group (Fig. 2).

Association of EA and PCT levels with other markers

We assessed the association of EA and PCT levels with other markers (Table 3). The WBC of the EA-H group was significantly lower than that of the EA-M group ($6.2\pm5.7\times10^3$ vs. $18.5\pm10.9\times10^3$; $P<0.05$), although there was no significant correlation between EA level and CRP. The CRP concentration of the PCT-L group was lower than that of the PCT-M and PCT-H groups (4.3±2.8 mg/dl (L). 17.8±9.5 mg/dl (M), 15.5±9.7 mg/dl (H), respectively), but this difference was not statistically significant. A significant correlation was found between PCT level and IL-6 blood level, although the EA level was not associated with the IL-6 blood level (Fig. 3). These results suggested that a high IL-6 level was associated with a high PCT level.

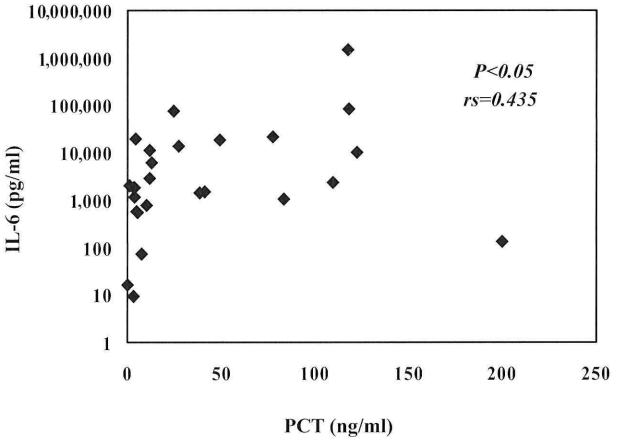

Fig. 3 Association of procalcitonin (PCT) with Interleukin (IL)-6. PCT has a significant positive correlation with IL-6.

Association of EA and PCT levels with the use of PMX-DHP

We further investigated the relationship between treatment with PMX-DHP and EA or PCT level. The rate of PMX-DHP application was 38.4% (5/14) for patients of the EA-L group, 20% (1/5) for patients of the EA-M group, and 35.7% (5/14) for patients of the EA-H group, respectively ; and 0% (0/4) for patients of the PCT-L group, 40% (4/10) for patients of the PCT-M group, and 36.8% (7/19) for patients of the PCT-H group, respectively (Fig. 4). There was no significant relationship between treatment with PMX-DHP and EA or PCT level. Although 5 out of 14 patients of the EA-L group had been treated with PMX-DHP, no patients of the PCT-L group were treated with PMX-DHP.

Discussion

The findings of this study indicated that the measurement of endotoxin activity (EA), procalcitonin (PCT) or interleukin(IL)-6 cannot predict the severity of illness and EA or PCT cannot predict the use of polymyxin B immobilized fiber column (PMX-DHP) treatment for patients with severe sepsis or septic shock admitted to the ICU. There was a significant correlation between PCT level and interleukin (IL)-6 blood level, which closely reflects the activation of the cytokine cascade and correlate well with the severity of clinical conditions, although PCT and IL-6 levels did not correlate with the APACHE II and SOFA score on admission.

Table 3 Illness severity and laboratory data at EA level and PCT level

	EA level			PCT level		
	L-group (n=13)	M-group (n=5)	H-group (n=15)	L-group (n=4)	M-group (n=10)	H-group (n=19)
APACHE II	23.9±7.8	25.0±7.5	26.4±8.1	22.3±10.2	25.8±7.6	25.5±7.6
SOFA	10.0±3.5	7.8±2.5	10.1±3.7	7.0±3.9	10.0±3.4	10.1±3.4
WBC (10^3/mm^3)	11.3±9.6	18.5±10.9	6.2±5.7*	11.2±6.2	14.0±10.6	7.8±8.3
CRP (mg/dl)	14.6±12.4	17.8±6.2	14.1±8.5	4.3±2.8	17.8±9.5	15.5±9.7
IL-6 (pg/ml)	1,665 (9-1,480,000) (n=10)	1,505 (536-21,800) (n=4)	4,510 (72-81,600) (n=12)	998 (16-1,980) (n=2)	764 (9-19,000) (n=9)	10,200 (131-1,480,000) (n=15)
ICU length of stay, days	14.2±2.9	10.0±1.7	6.9±1.2	8.5±1.6	11.9±2.8	10.1± 2.1
Mortality, number. (%)	4 (30.8%)	1 (20.0%)	5 (33.3%)	0 (0%)	4 (40.0%)	6 (31.6%)

Continuous parameter data are expressed as means±SD. Discontinuous parameter data are expressed as median values (minimum to maximum) ; APACHE, Acute Physiology and Chronic Health Evaluation ; SOFA, Sepsis-related Organ Failure Assessment ; EA, Endotoxin activity ; PCT, Procalcitonin ; CRP, C-reactive protein ; IL-6, Interleukin-6 ; WBC, White blood cell count ; ICU, intensive care unit ; EA level : L-group (<0.4), M-group (0.4≤ <0.6), H-group (≥0.6) ; PCT level : L-group (<2 ng/ml), M-group (2≤<10 ng/ml), H-group (≥10 ng/ml)

*P<0.05 vs patients with EA level M-group

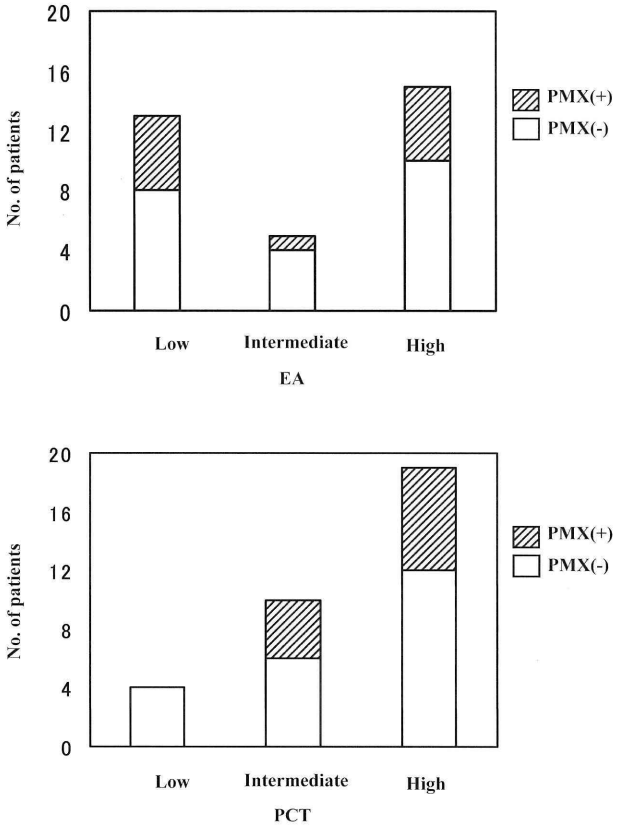

Fig. 4 Association of endotoxin activity (EA) and procalcitonin (PCT) levels with the use of PMX-DHP. There was no significant relationship between treatment with PMX-DHP and EA or PCT level. Shaded columns represent the number of patients with PMX-DHP, while empty columns represent the number of patients without PMX-DHP. EA, Endotoxin activity assay ; PCT, Procalcitonin ; PMX, polymixin B immobilized fiber column, EA-low (EA level <0.4), EA-intermediate (0.4≤EA level<0.6), EA-high (EA level≥0.6) ; PCT-low (PCT level<2 ng/ml), PCT-intermediate (2 ng/ml≤PCT level <10 ng/ml), PCT-high (PCT level ≥10 ng/ml).

Sepsis is a condition that exhibits various symptoms of systemic inflammatory response due to collapse of immunological defenses against local infections, and the number of cases of this disease has increased in recent years. There are several reasons for the growing number of cases of sepsis, namely, an increase in the number of aged people, immunocompromised patients with complications of diabetes and malignant growth, and invasive therapies and examinations. If the patient condition deteriorates from severe sepsis to septic shock, and multiple organ failure (MOF) develops, the survival rate is low. It was suggested that one reason for the high mortality of severe sepsis could be the failure of early diagnosis in the acute phase, when multimodality therapy is effective. Furthermore, it was suggested that it is difficult to appropriately control the activated inflammatory response. Therefore, rapid and accurate diagnosis, as well as initiation of appropriate treatment in intensive care are important for sepsis treatment. Endotoxin plays an important role in innate immunity and also causes the production of various mediators linked to MOF or disseminated intravascular coagulation. In Japan, highly sensitive detection methods with kinetic turbidimetric assay (LAL) are widely used for endotoxin assay. However, this method is not completely reliable in the clinical setting because of difficulties relating to preparation and extraction. LPS binds to a number of plasma circulating inhibitors of the coagulation reaction, such as lipopolysaccharide binding protein, soluble CD14, CD11b/CD18 integrin receptors, and high density lipoprotein, and to cellular blood components such as platelets. Moreover, the assay is not specific for endotoxin because the limulus coagulation cascade can be activated by fungal products.

In the present study, we measured endotoxin level using EAA (FDA-approved) for endotoxin assay. The advantage of EAA for clinical use is that it can be assayed rapidly within 30 min from whole blood without complex pretreatment. Marshall et al. reported that EAA was useful in critically ill patients with suspected sepsis and that increased EA level at admission was associated with the development of severe sepsis and organ dysfunction[14]. Another study reported that higher levels of endotoxin revealed by EAA in patients after surgery were associated with a longer stay in the ICU[18]. Moreover, at the same time we also measured PCT levels, which were closely related to the bacterial infection and were assumed to correlate with the severity of bacterial infection. Several clinical studies have indicated that PCT was more sensitive and more specific in discriminating between patients with or without sepsis than any other established blood markers[19]. PCT is induced in the circulation within 2 to 4 h after bacterial infection, and its half-life is estimated to be approximately from 24 to 30 h. CRP is an acute phase protein used mostly as an inflammatory marker. However, its concentration does not significantly increase until 24 h after the onset of inflammation and is not specific for infectious disease. Because PCT is a substance that is released more rapidly than CRP, the former is an early indicator for the existence of bacterial infection.

The aim of the present study was to investigate whether the measurement of EA and PCT levels can predict further intensive care application for patients with severe sepsis or septic shock, because it has been reported that EA levels correlated with the severity of sepsis and gram-negative infection and PCT levels correlate with the severity of bacterial infection. In other words, high levels of both markers would indicate severe bacterial infection with gram-negative bacteria. In addition, both markers are readily available in clinical laboratories and diagnostic assays can be performed approximately within

30 min. It should be possible to rapidly recognize and risk-stratify patients with suspected sepsis, and to guide therapy for endotoxin. In Japan, the clinical usefulness of PMX-DHP has been reported in septic shock patients with gram-negative infection[20] and it is more important to know when this therapy should be initiated. Recently, multicenter RCT on PMX-DHP therapy was performed in patients with septic shock and severe sepsis induced by abdominal sepsis[21]. In this study, PMX-DHP significantly improved hemodynamics and organ dysfunction and reduced 28-day mortality. However, the results of this study did not show any significant correlation between the severity of illness with EA or PCT level and between EA level and gram-negative infection. Furthermore, there was no relationship between the implementation of PMX-DHP treatment and the measurement of EA and PCT levels. The reason for the lack of the correlation between the pathogen and EA levels may be that patients severely infected with gram-positive bacteria could have a high level of EA and some patients infected with gram-negative bacteria could have a low level of EA. This may suggest that the reactivity of neutrophils could be suppressed in patients receiving high doses of steroids, and the EA level could depend on the function of individual neutrophils, because neutrophils are used in the assay. High-dose administration of steroid might suppress the PCT level. Moreover, EAA detects the level of endotoxin, which is located in the upstream from the inflammation cascade. On the other hand, it is also thought that PCT is located downstream from the inflammation cascade, since PCT is thought to be released by endotoxin stimulation or direct stimulation of bacterial products. The present study showed good correlation between PCT levels and IL-6 blood levels. This may support the theory that PCT is produced immediately from the various systemic organs stimulated by proinflammatory cytokines such as TNF-α and IL-6. Therefore, it may not be rational to evaluate the levels of both EA and PCT at the same time. The limitations of this study are as follows. (1) The small number of patients. (2) Various underlying diseases apart from severe sepsis as the subject. (3) Some patients were prescribed antimicrobial agents before ICU admission, which could affect EA and PCT levels. Further study involving the evaluation of a larger study group is required.

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重症敗血症における endotoxin activity assay および procalcitonin の役割

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目的：集中治療室（ICU）へ入室した重症敗血症患者の重症度と endotoxin activity（EA）、プロカルシトニン（procalcitonin : PCT）およびインターロイキン-6（IL-6）との関連を調査し、EA および PCT がエンドトキシン吸着療法である PMX-DHP 開始の指標となるかを検討した。

対象および方法：重症敗血症または敗血症性ショックにて ICU へ入室した 33 名を対象とした。入室 6 時間以内に EA、PCT、IL-6 および一般血液検査等を行い、重症度評価には Acute Physiology and Chronic Health Evaluation II（APACHE II）スコアと Sepsis-related Organ Failure Assessment（SOFA）スコアを用いた。患者を EA および PCT の値によってそれぞれ低値群（L 群）、中間値群（M 群）、高値群（H 群）の 3 群に階層化し、各種パラメータとの関連および PMX-DHP 施行との関連について検討した。

結果：APACHE II スコア、SOFA スコアとも EA、PCT および IL-6 との間には明らかな関連は認めなかったが PCT と IL-6 には有意な相関を認めた。グラム陰性菌感染患者の EA は 0.58±0.19、グラム陽性菌患者は 0.45±0.22 であり有意差は認めなかった。PMX-DHP 施行率は、EA-L 群 38.4%（5/14）、M 群 20%（1/5）、H 群 35.7%（5/14）、PCT-L 群 0%（0/4）、M 群 40%（4/10）、H 群 36.8%（7/19）であった。

結語： EA はグラム陰性菌感染および疾患重症度とは関連を認めなかった。PCT および IL-6 も疾患重症度とは関連を認めなかったが、PCT と IL-6 は良い相関を認めた。PMX-DHP 施行の指標として、EA および PCT 測定の有用性は認められなかった。

〈キーワード〉　エンドトキシン活性、プロカルシトニン、重症敗血症、PMX-DHP