원 저

Clinical Identifiers and Pathogenic Significance of *Pseudomonas aeruginosa* Bacteremia, in Comparison with *Klebsiella pneumoniae* and *Enterobacter* species

Cheol-In Kang, M.D.[1], Sung-Han Kim, M.D.[1], Ji-Whan Bang, M.D.[1], Hong-Bin Kim, M.D.[1]
Nam-Joong Kim, M.D.[1], Eui-Chong Kim, M.D.[2,3], Myoung-don Oh, M.D.[1,3], and Kang-Won Choe, M.D.[1,3]
[1]Departments of Internal Medicine and [2]Laboratory Medicine, Seoul National University College of Medicine
[3]Clinical Research Institute, Seoul National University Hospital, Seoul, Republic of Korea

녹농균 균혈증의 임상적인 감별 특성 및 병원체로서의 중요성 : 폐렴 간균, 엔테로박터균과의 비교 연구

서울대학교 의과대학 내과학교실[1], 진단검사의학교실[2], 서울대병원 임상의학연구소[3]
강철인[1] · 김성한[1] · 방지환[1] · 김홍빈[1] · 김남중[1] · 김의중[2,3] · 오명돈[1,3] · 최강원[1,3]

Background : To identify specific risk factors for *Pseudomonas aeruginosa* and evaluate the relationship between the mortality rate and *P. aeruginosa* bacteraemia in bloodstream infections, we compared the clinical features and outcomes of patients with *P. aeruginosa* bacteremia with the patients with *Klebsiella pneumoniae* or Enterobacter bacteremia.

Materials and Methods : A total of 190 patients with *P. aeruginosa* bacteremia were identified from January 1998 to December 2002 and included in this retrospective analysis. During the same period, 377 patients with *K. pneumoniae* bacteremia and 183 patients with Enterobacter bacteremia were identified and compared with those with *P. aeruginosa* bacteremia.

Results : Factors associated with *P. aeruginosa* bacteremia in the multivariate analysis included pneumonia, soft tissue infection, nosocomial acquisition, neutropenia, and prior invasive procedure (All $P<0.05$). The 30-day mortality rate was 37.9% (72/190) in patients with *P. aeruginosa* bacteremia, 24.1% (91/377) in those with *K. pneumoniae*, and 25.7% (47/183) in those with Enterobacter bacteremia ($P<0.001$). However, in the analysis including patients who had received appropriate initial antimicrobial therapy (n=552), the mortality rate of *P. aeruginosa* bacteremia was not significantly higher than that of non-pseudomonas bacteremia (28.6% [18/63] vs. 22.5% [110/489]; $P=0.282$). Inappropriate initial antimicrobial therapy was found to be one of the significant independent predictors of mortality. *P. aeruginosa* bacteremia as a risk factor for mortality did not reach statistical significance (OR, 1.30; 95% CI, 0.73-2.32; $P=0.371$), after adjusting for underlying illness and adequacy of antimicrobial therapy.

Conclusion : An initial empirical antimicrobial coverage of *P. aeruginosa* should be seriously considered in patients with pneumonia, soft tissue infection, neutropenia, and prior invasive procedure, when gram-negative sepsis was suspected in nosocomial infection.

Key Words : *Pseudomonas aeruginosa,* Gram-Negative Bacterial Infections, Bacteremia, Treatment Outcome, Risk Factor

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Correspondence : Myoung-don Oh, M.D.
Department of Internal Medicine, Seoul National University College of Medicine
28 Yongon-dong Chongno-gu, Seoul, 110-744, Korea
Tel : +82-2-2072-2945, Fax : +82-2-762-9662, E-mail : mdohmd@snu.ac.kr

INTRODUCTION

Pseudomonas aeruginosa remains one of the most feared organisms that cause bacteremia (1, 2). Nevertheless, as the symptoms of *P. aeruginosa* bacteremia are nonspecific, the initial antimicrobial therapy for possible *P. aeruginosa* bacteremia is almost always empirical, with a pending identification of the responsible pathogens (3). Inappropriate antimicrobial therapy of bacteremia is associated with a significantly poorer outcome (4-7). In addition, this pathogen has repeatedly been found to bear an adverse prognostic potential (8-10). It is therefore important to determine the likelihood of *P. aeruginosa* bacteremia as a cause of particular infection syndrome. Answering this question would help clinicians choose the most adequate empirical treatment in clinical situations that include *P. aeruginosa* bacteremia as a possible cause.

Examination of published mortality figures over an 8-year period showed widely different rates, but even more recent publications show attributable mortality rates of 28% to 44%, depending on the adequacy of treatment and seriousness of the underlying diseases (1, 11-14). However, in a matched cohort of non-neutropenic patients, mortality attributable to *P. aeruginosa* infection has been reported to be low, 15% (1, 15). Whether such low rates are a reflection of early appropriate therapy or differences in the populations examined is not known (1, 15). The mortality associated with severe *P. aeruginosa* infections may be high for several reasons; the population most at risk for *P. aeruginosa* bacteremia includes the sickest and most compromised group of hospitalized individuals, and *P. aeruginosa* infection is associated with a greater likelihood of inappropriate antimicrobial therapy (1, 16).

For all these reasons, it seems appropriate for us to gather and report additional data on clinical identifiers and pathogenic significance of *P. aeruginosa* in bloodstream infections. Thus we performed a large retrospective study to determine risk factors for *P. aeruginosa* bacteremia. To identify specific risk factors for *P. aeruginosa* bacteremia, we included in our study a control group of patients with bacteremia due to *K. pneumoniae* or *Enterobacter* spp., which at our institution remain the medically-important gram-negative bacilli frequently isolated from blood and from severe infections. We also investigated whether the presence of *P. aeruginosa* represented an independent adverse prognostic factor.

MATERIALS AND METHODS

1. Patients and bacterial strains

The database at our Clinical Microbiology Laboratory (Seoul National University Hospital, Seoul, Korea) was reviewed in order to identify patients with *P. aeruginosa* bacteremia. Patients older than 16 years of age with *P. aeruginosa* bacteremia were included in the analysis. Only the first bacteremic episode for each patient was included in the analysis. We reviewed the medical records of individuals diagnosed from January 1998 to December 2002 at Seoul National University Hospital, Seoul, Korea, a 1500-bed tertiary care university hospital and referral center. The episodes of *P. aeruginosa* bacteremia were compared with those due to *Klebsiella pneumoniae* and *Enterobacter* spp. that occurred among our patients during the same period, since these strains are the medically-important gram-negative bacilli comparable to *P. aeruginosa*. Species identification was carried out with Vitek-GNI Card (bioMérieux, Hazelwood, MO) by standard methods, and antibiotic susceptibility testing was performed using the disk diffusion method, following the recommendations of the National Committee for Clinical Laboratory Standards (17, 18).

2. Study design and data collection

We reviewed the medical records of the patients and compared data from patients with *P. aeruginosa* bacteremia with data from those with non-pseudomonas bacteremia (*K. pneumoniae* and *Enterobacter* spp.). The data collected included age, gender, underlying disease, primary site of infection, severity of illness as calculated by the Acute Physiology and Chronic Health Evaluation (APACHE) II score (19), and the antimicrobial therapy regimen. The presence of the following comorbid conditions was also documented: neutropenia, presentation with septic shock, care in intensive care unit (ICU), receipt of immunosuppressive agents within

30 days prior to the bacteremia, corticosteroid use, the presence of a central venous catheter or of an indwelling urinary catheter, and post-operative state. As this study was retrospective, the patients' physicians, not the researchers, had chosen the antimicrobial therapy regimens. The main outcome measure used was the 30-day mortality rate.

3. Definitions

Bacteremia was defined as the isolation of causative microorganism in a blood culture specimen. Clinically significant bacteremia was defined as at least one positive blood culture, together with clinical features compatible with systemic inflammatory response syndrome. The initial antimicrobial therapy was considered 'appropriate' if the initial antibiotics, which were administered within 24 hours after acquisition of a blood culture samples, included at least one antimicrobial agent that was active in vitro against the causative microorganisms, and when the dosage and route of administration conformed with current medical standards. 'Inappropriate initial antimicrobial therapy' referred to the administration of antimicrobial agents to which the causative microorganisms were resistant *in vitro*, or to the lack of an antimicrobial therapy for a known causative pathogen. If the antimicrobial agent was not administered within 24 hours of bacteremia onset, then antimicrobial use was considered inappropriate. As aminoglycoside was not prescribed at high dose, once daily dosing which might be appropriate for *P. aeruginosa* bacteremia, aminoglycoside monotherapy was considered as an inappropriate therapy for *P. aeruginosa*. The primary site of infection was determined on the basis of the isolation of microorganisms from the presumed portal of entry and clinical evaluation (20). The bacteremia was categorized as polymicrobial if additional microorganisms were recovered from the blood cultures. Nosocomial infection was defined as an infection that occurred ≥48 h after hospital admission; an infection that occurred <48 h after admission to the hospital, in patients that had been hospitalized in the 2 weeks prior to admission; and an infection that occurred <48 h after admission to the hospital in patients that had been transferred from another hospital or nursing home. Neutropenia was defined as an absolute neutrophil count below 500/mm^3. Septic shock was defined as sepsis associated with evidence of organ hypoperfusion and a systolic blood pressure <90 or >30 mm Hg less than the baseline or a requirement for the use of vasopressor to maintain blood pressure.

4. Statistical analysis

The Student's t-test was used to compare continuous variables, and χ^2 or Fisher's exact test to compare categorical variables. In identifying the independent risk factors, a backward stepwise logistic regression analysis was used to control for the effects of confounding variables and variables with a *P*-value <0.10 in the univariate analysis were candidates for multivariate analysis. We used backward elimination of any variable that did not contribute to the model on the grounds of the likelihood ratio test, using a significance cutoff of 0.05. All *P*-values were two-tailed, and *P*-values<0.05 were considered statistically significant. The SPSS for windows, version 11.5 software package (SPSS Inc, Chicago, Ill), was used for all analyses.

RESULTS

1. Study population and demographic characteristics

During the study period, a total of 190 patients with *P. aeruginosa* bacteremia were identified and included in the analysis. The mean (±standard deviation) patient age was 54±16 (range, 15-95 years) and 129 (67.9%) patients were male. The most common underlying diseases were neoplastic diseases (hematologic malignancy and solid tumor, 68.4%). During the same period, 377 patients with *K. pneumoniae* bacteremia and 183 patients with Enterobacter bacteremia were identified and compared with those with *P. aeruginosa* bacteremia. Table 1 compares demographic characteristics for patients with *P. aeruginosa* versus *K. pneumoniae* or Enterbacter bacteremia. The patients with underlying neoplastic diseases were significantly more frequent in *P. aeruginosa* group than non-pseudomonas group (68.4 % [130/190] vs. 48.4% [271/560], *P*<0.001). However, the 32.4% of patients with *K. pneumoniae* bacteremia had chronic liver diseases such as cirrhosis, whereas only 1.6% of those with *P. aeruginosa* bacteremia had chronic liver diseases (*P*<0.001). When assessed the

Table 1. Demographic Characteristics of Study Population

	P. aeruginosa (n=190)	*K. pneumoniae* (n=377)	*Enterobacter* species. (n=183)
Age, mean year±SD (range)	54±16 (15-95)	55±13 (17-89)	54±15 (16-85)
Male	129 (67.9)	249 (66.0)	105 (57.4)
Underlying diseases			
Hematologic malignancy	46 (24.2)	60 (15.9)	39 (21.3)
Solid tumor	84 (44.2)	97 (25.7)	75 (41.0)
Solid organ transplantation	4 (2.1)	5 (1.3)	9 (4.9)
Chronic liver diseases	3 (1.6)	122 (32.4)	12 (6.6)
Benign pancreaticobiliary tract disease	14 (7.4)	31 (8.2)	10 (5.5)
Chronic renal diseases	7 (3.7)	6 (1.6)	7 (3.8)
Others	28 (14.7)	28 (7.4)	25 (13.7)
None	2 (1.1)	13 (3.4)	2 (1.1)
Primary site of infection			
Pancreaticobiliary tract	54 (28.4)	89 (23.6)	53 (29.0)
Liver	0 (0)	25 (6.6)	3 (1.6)
Lung	31 (16.3)	21 (5.6)	7 (3.8)
Urinary tract	20 (10.5)	32 (8.5)	18 (9.8)
Peritoneum	5 (2.6)	82 (21.8)	18 (9.8)
Soft tissue	13 (6.8)	3 (0.8)	2 (1.1)
Catheter-related	9 (4.7)	0 (0)	8 (4.4)
Unknown	57 (30)	125 (33.2)	73 (39.9)

Data represent patient numbers (%), otherwise indicated.
SD, standard deviation

Table 2. Underlying Conditions of Study Population

	P. aeruginosa (n=190)	*K. pneumoniae* (n=377)	*Enterobacter* spp. (n=183)	*P**
Nosocomial acquisition	151 (79.5)	186 (49.3)	145 (79.2)	<0.001
Neutropenia	54 (28.4)	70 (18.6)	40 (21.9)	0.011
Presentation with septic shock	46 (24.2)	92 (24.4)	50 (27.3)	0.753
ICU care	23 (12.1)	14 (3.7)	31 (16.9)	0.091
Immunosuppressant use	15 (7.9)	16 (4.2)	20 (10.9)	0.488
Corticosteroid use	42 (22.1)	44 (11.7)	37 (20.2)	0.014
Post-surgical state	16 (8.4)	13 (3.4)	29 (15.8)	0.681
Polymicrobial infection	24 (12.6)	40 (10.6)	25 (13.7)	0.706
Indwelling urinary catheter	39 (20.5)	40 (10.6)	44 (24.0)	0.075
Central catheterization	46 (24.2)	66 (17.5)	65 (35.5)	0.819
Prior invasive procedure within 72 hours†	49 (25.8)	32 (8.5)	39 (21.3)	<0.001
Prior use of antibiotics	91 (47.9)	105 (27.9)	83 (45.4)	<0.001
APACHE II score, mean±SD (range)	11.8±4.6 (0-26)	10.8±4.9 (0-28)	12.0±5.0 (0-25)	0.099

NOTE. Data represent patient numbers (%), otherwise indicated.
*Comparison of *P. aeruginosa* bacteremia vs. non-pseudomonas bacteremia
†invasive procedure such as endoscopic retrograde cholangiopancreaticography, endoscopic sphincterotomy, percutaneous drainage, or hemodialysis
ICU, intensive care unit; APACHE: Acute Physiology and Chronic Health Evaluation

primary sites of infection, lung and soft tissue were significantly more common in *P. aeruginosa* bacteremia than non-pseudomonas bacteremia (16.3% [31/190] vs. 5.0% [28/560], $P<0.001$; 6.8% [13/190] vs. 0.9% [5/560], $P<0.001$, respectively).

2. Clinical identifiers associated with *P. aeruginosa* bacteremia

Among the patients with *P. aeruginosa* bacteremia, eighty percent of the patients had nosocomial infection and 28.4% of the patients were neutropenic state. Forty eight percent of the patients had a prior use of antibiotics within 30 days before bacteremia. The clinical characteristics of the population analyzed are summarized in Table 2. Nosocomial acquisition, neutropenia, corticosteroid use, prior invasive procedure, and prior use of antibiotics were more frequent in *P. aeruginosa* bacteremia, compared with non-pseudomonas bacteremia

(All $P<0.05$, Table 2). Factors that were also independently predictive for *P. aeruginosa* bacteremia in the multivariate analysis included pneumonia, soft tissue infection, nosocomial acquisition, neutropenia, and prior invasive procedure within 72 hours before onset of bacteremia (Table 3).

3. Treatment outcomes and risk factors for mortality

Of 190 patients with *P. aeruginosa* bacteremia, only 63 (33.2%) received appropriate initial antimicrobial therapy. To the contrary, 91.2% of patients with *K. pneumoniae* bacteremia and 79.2% of those with Enterobacter bacteremia, respectively, received appropriate initial antimicrobial therapy. Table 4 summarizes the results of clinical outcome analysis. The 30-day mortality rate was 37.9% (72/190) in patients with *P. aeruginosa* bacteremia, 24.1% (91/377) in those with *K. pneumoniae*, and 25.7% (47/183) in those with Enterobacter bacteremia (5, 21). Patients with *P. aeruginosa* bacteremia had a significantly higher mortality when compared with the non-pseudomonas group (37.9% [72/190] vs. 24.6% [138/560]; $P<0.001$). However, in the analysis of patients who received appropriate initial antimicrobial therapy (n=552), the 30-day mortality rate was 28.6% (18/63) in patients with *P. aeruginosa* bacteremia, 21.8% (75/344) in those with *K. pneumoniae* bacteremia, and 24.1% (35/145) in those with Enterobacter bacteremia. In this subgroup analysis, the mortality of *P. aeruginosa* bacteremia was not significantly higher than that of non-pseudomonas bacteremia (28.6% [18/63] vs. 22.5% [110/489]; $P=0.282$). In patients with *P. aeruginosa* bacteremia, the appropriate initial antimicrobial therapy group had a 28.6% mortality rate, whereas the inappropriate therapy group had a 42.5% mortality rate ($P=0.062$).

Table 5 shows the results of stratified analysis of

Table 3. Clinical Identifiers Associated with *P. aeruginosa* in Bloodstream Infections

	Adjusted OR (95% CI)	*P*
Pneumonia	4.84 (2.75-8.53)	<0.001
Soft tissue infection	8.92 (3.01-26.41)	<0.001
Prior invasive procedure within 72 hours*	2.73 (1.71-4.35)	<0.001
Nosocomial acquisition	2.06 (1.35-3.15)	0.001
Neutropenia	1.81 (1.18-2.76)	0.006

Multivariate analysis using a logistic regression model included the following variables: underlying malignancy, pneumonia, soft tissue infection, nosocomial acquisition, neutropenia, ICU care, corticosteroid use, indwelling urinary catheter, prior invasive procedure, prior use of antibiotics
*invasive procedure such as endoscopic retrograde cholangiopancreaticography, endoscopic sphincterotomy, percutaneous drainage, or hemodialysis

Table 4. Comparison of Clinical Outcomes in *P. aeruginosa* Bacteremia Versus Non-pseudomonas Bacteremia

	P. aeruginosa	*K. pneumoniae*	*Enterobacter* spp.	*P**
3-day mortality	12.6% (24/190)	10.9% (41/377)	6.6% (12/183)	0.214
7-day mortality	19.5% (37/190)	14.9% (56/377)	16.4% (30/183)	0.185
30-day mortality	37.9% (72/190)	24.1% (91/377)	25.7% (47/183)	<0.001

*Comparison of *P. aeruginosa* bacteremia vs. non-pseudomonas bacteremia

Table 5. Stratified Analysis of 30-day Mortality Rates of Pseudomonas bacteremia vs. non-Pseudomonas bacteremia and Inappropriate Initial Antimicrobial Therapy Group vs. Appropriate Therapy Group, According to the Presence of Septic Shock at Initial Presentation and APACHE II Score

	Causative microorganisms			Initial antimicrobial therapy		
	Pseudomonas	Non-Pseudomonas	*P*	Inappropriate	Appropriate	*P*
Septic shock*						
No (n=562)	34/144 (23.6)	35/418 (8.4)	<0.001	36/143 (25.2)	33/419 (7.9)	<0.001
Yes (n=188)	38/ 46 (82.6)	103/142 (72.5)	0.170	46/ 55 (83.6)	95/133 (71.4)	0.079
APACHE II score						
≤8 (n=201)	9/ 45 (20.0)	12/156 (7.7)	0.260	10/ 58 (17.2)	11/143 (7.7)	0.045
9-15 (n=401)	38/101 (37.6)	58/300 (19.3)	<0.001	42/ 95 (44.2)	54/306 (17.6)	<0.001
16≤ (n=148)	25/ 44 (56.8)	68/104 (65.4)	0.324	30/ 45 (66.7)	63/103 (61.2)	0.524

Data are the number of death/number of patients (%), unless otherwise indicated.
*Septic shock at initial presentation
APACHE, Acute Physiology and Chronic Health Evaluation

30-day mortality rates of Pseudomonas bacteremia vs. non-Pseudomonas bacteremia and inappropriate initial antimicrobial therapy group vs. appropriate therapy group, according to the presence of septic shock at initial presentation and APACHE II score.

Multivariate analysis using a logistic regression model, including the variables associated with mortality by univariate analysis (P<0.10), showed that the significant independent risk factors for mortality were; long hospital stay, having pneumonia, presentation with septic shock, inappropriate initial antimicrobial therapy, and an increasing APACHE II score (Table 6). *P. aeruginosa* bacteremia as a risk factor for mortality did not reach statistical significance (OR, 1.30; 95% CI, 0.73-2.32; P=0.371), after adjusting for underlying illness and adequacy of antimicrobial therapy. However, in the multivariate analysis excluding the inappropriate antimicrobial therapy variable, *P. aeruginosa* was found to be an independent predictor of death in our study (OR, 2.24; 95% CI, 1.38-3.64; P=0.001).

DISCUSSION

In this study we identified several potential risk factors for *P. aeruginosa* bacteremia, compared with *K. pneumoniae* or Enterobacter bacteremia. Multivariate analysis revealed that pneumonia, soft tissue infection, nosocomial acquisition, neutropenia, and prior invasive procedure were significantly associated with *P. aeruginosa* infection. The present data provide independent risk factors for these pathogens that allow us to predict the patient particularly at risk and, therefore, to select individual initial empirical antimicrobial therapy more judiciously. Our data suggest that an initial empirical antimicrobial coverage of *P. aeruginosa* should be seriously considered in patients with pneumonia, soft tissue infection, neutropenia, or prior invasive procedure, when gram-negative sepsis was suspected in nosocomial infection. However, therapeutic selection should also be based on the severity of the infection, knowledge of epidemiology and resistance phenotypes in individual settings, and the required pharmacokinetic-pharmacodynamic parameters (2).

Table 6. Independent Risk Factors for 30-day Mortality

	Adjusted OR (95% CI)	*P*
Presentation with septic shock	23.20 (14.08-38.21)	<0.001
Pneumonia	4.53 (2.22-9.25)	<0.001
Inappropriate initial antimicrobial therapy	3.23 (1.98-5.26)	<0.001
Long hospital stay (>14 days)*	1.91 (1.19-3.05)	0.007
Increased APACHE II score (per 1-point increments)	1.21 (1.41-1.27)	<0.001

Multivariate analysis using a logistic regression model included the following variables: long hospital stay, pneumonia, presentation with septic shock, ICU care, corticosteroid use, immunosuppressant use, inappropriate antimicrobial therapy, *P. aeruginosa* bacteremia, and APACHE II score.
*Hospital stay prior to onset of bacteremia

Despite the common occurrence of bloodstream infections among hospitalized patients, few studies have attempted to compare the influence of bloodstream infections due to specific pathogens on mortality (10, 22-23). Our study is unique in examining this association among patients with *P. aeruginosa* bacteremia and other gram-negative bacteremia such as *K. pneumoniae* or *Enterobacter* spp. Our study confirms the adverse prognostic potential of *P. aeruginosa* bacteremia, compared with *K. pneumoniae* or Enterobacter bacteremia. Mortality in patients with *P. aeruginosa* bacteremia was 38%, compared with 25% in the non-pseudomonas group.

In our study, fewer patients with *P. aeruginosa* bacteremia were appropriately treated than were patients with non-pseudomonas bacteremia. Moreover, we also observed, as reported in our other study (5), a significant association between survival and administration of an antimicrobial agent to which the strain was susceptible *in vitro*. These data may explain, at least in part, the high acute and crude mortality rates among *P. aeruginosa*-infected patients. The overall mortality rate of *P. aeruginosa* bacteremia was 38%, with rates of 29% for patients that received appropriate antimicrobial therapy and 43% for patients that received inappropriate antimicrobial therapy. Thus, 14% reduction in the overall crude mortality rate was associated with adequate early empiric antimicrobial therapy. Moreover, *P. aeruginosa* bacteremia failed to be an independent predictor of death in our study, after adjusting for underlying illness and adequacy of antimicrobial therapy. Our data suggest that it is likely that excess mortality observed in the *P. aeruginosa* group is

directly attributable to inadequacy of antimicrobial therapy. Furthermore, in the patients who received appropriate initial antimicrobial therapy, the mortality of patients with *P. aeruginosa* bacteremia was comparable to that of those with non-pseudomonas bacteremia. Since comorbidity (i.e. APACHE Ⅱ score and septic shock) in patients with and without *P. aeruginosa* was comparable, it is likely that excess mortality observed in the *P. aeruginosa* group is directly attributable to these pathogens and inadequacy of antimicrobial therapy. Nevertheless, since this study was of retrospective nature, we cannot fully exclude that the severity of comorbidity to some extent may represent a confounder.

Although the 30-day mortality of *P. aeruginosa* bacteremia was significantly higher, there was no significant difference in the 3-day mortality between Pseudomonas group and non-pseudomonas group. In addition, there were no significant differences in the 30-day mortality rates of Pseudomonas group vs. non-Pseudomonas group and inappropriate initial antimicrobial therapy group vs. appropriate therapy group, in the subgroup analysis including severely-ill patients (e.g. APACHE Ⅱ score≥16 or septic shock at initial presentation). One reasonable hypothesis is that some patients are so sick that they will die within the several days following bacteremia, independently of any antimicrobial therapy or causative microorganisms (14). In contrast, patients in better clinical condition at the time of bacteremia might survive a few days independently of the appropriateness of antimicrobial therapy (13, 14). Evidence supporting this hypothesis comes from the observation that clinical presentation and underlying illness at the onset of bacteremia is the strongest independent indicator of survival (5, 13, 14).

It is important to note that our study does not prove a causal relationship between bloodstream infections and 30-day mortality. However, our analysis suggests that the prevention of bloodstream infections and improvement in the management of patients with bloodstream infections may reduce mortality, especially in *P. aeruginosa* bacteremia.

As this study was of the retrospective nature, the possibility of the limitation in precluding accurate comparisons should be borne in mind. The data were limited to the hospital record. Also, we only compared patients with *P. aeruginosa* bacteremia with those with *K. pneumoniae* or Enterobacter bacteremia. It is possible that bloodstream infections associated with other pathogens could have produced different results. Indeed, in other study regarding *P. aeruginosa* and *Staphylococcus aureus* bacteremia (10), the patients with *P. aeruginosa* bacteremia have a greater risk of mortality compared with *S. aureus* bacteremia despite appropriate antimicrobial therapy. Finally, our study was conducted in a large tertiary care medical center, thus the results may not be applicable to other institutions.

In conclusions, our study revealed that pneumonia, soft tissue infection, nosocomial acquisition, neutropenia, and prior invasive procedure were significantly associated with *P. aeruginosa* infection. The mortality rate of patients with *P. aeruginosa* bacteremia was significantly higher than that of patients with *K. pneumoniae* or Enterobacter bacteremia. However, in patients who received appropriate initial antimicrobial therapy, the mortality rate of *P. aeruginosa* bacteremia was comparable to that of non-pseudomonas bacteremia. Inappropriate initial antimicrobial therapy was found to be one of the significant independent predictors of mortality. An initial empirical antimicrobial coverage of *P. aeruginosa* should be seriously considered in patients with pneumonia, soft tissue infection, neutropenia, or prior invasive procedure, when gram-negative sepsis was suspected in nosocomial infection.

ABSTRACT

목 적 : 그람 음성 균혈증 환자들 중 녹농균 감염의 임상적인 감별 특성을 파악하고 사망율과의 관계를 평가하기 위해서, 녹농균 균혈증 환자들의 임상적 특성과 치료결과를 폐렴 간균, 엔테로박터균 균혈증 환자들과 비교하였다.

재료 및 방법 : 1998년 1월 부터 2002년 12월까지 발생한 총 190명의 녹농균 균혈증 환자들이 연구에 포함되었다. 같은 기간 동안 377명의 폐렴 간균, 183명의 엔테로박터균 균혈증 환자들이 확인되어 녹농균 균혈증 환자들과 비교 연구되었다.

결 과 : 다변량 분석에서 녹농균 균혈증과 관련 있는 것으로 나타난 독립적인인자들로는 폐렴, 연부조직 감염, 병원 감염, 호중구 감소증, 이전에 침습적인 시술을 받은 경우가 있었다(All $P<0.05$). 녹농균 균혈증 환자들의 30일

사망율은 37.9% (72/190)였고, 폐렴 간균 균혈증 환자들의 사망율은 24.1% (91/377), 엔테로박터균 균혈증 환자들의 사망율은 25.7% (47/183)이었다. 하지만, 초기에 적절한 항생제를 투여받은 환자들을 따로 분석하였을 때(n=552), 녹농균 균혈증 환자들의 사망율이 다른 균혈증 환자들에 비해 유의하게 높지는 않았다(28.6% [18/63] vs. 22.5% [110/ 489]; P=0.282). 초기 부적절한 항생제 투여는 사망의 독립적인 위험인자들 중 하나로 나타났다. 사망의 독립적인 위험인자로서 녹농균 균혈증은 기저 질환과 초기 항생제의 적정성 등을 보정한 후 통계적인 유의성을 보이지 않았다(OR, 1.30; 95% CI, 0.73-2.32; P=0.371).

결 론 : 병원 감염에서 그람음성 균주에 의한 균혈증이 의심될 때, 특히 폐렴, 연부 조직 감염, 호중구 감소증, 이전에 침습적인 시술을 받은 환자들에서는 녹농균에 효과가 있는 경험적 항생제 투여를 신중하게 고려해야 한다.

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