Risk Factors for *Pseudomonas aeruginosa* Bacteremia in Thai Patients†

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Abstract

A case control study to determine the risk factors for *P. aeruginosa* bacteremia was conducted in patients admitted to Siriraj Hospital in 1998.

The case group consisted of 65 patients with *P. aeruginosa* bacteremia. There were 3 control groups. 65 patients with *E. coli* bacteremia, 64 patients with *S. aureus* bacteremia and 65 patients without bacteremia. Demographic information and potential risk factors i.e. type of infection, associated diseases/conditions, procedures/surgery, previous/current use of antibiotics and previous/current use of immunosuppressive/cytotoxic agents were extracted from the patients' medical records and compared. Univariate analysis revealed that the factors associated with *P. aeruginosa* bacteremia were infections acquired while hospitalized, hematologic malignancy, neutropenia, COPD, antibiotic receivers, cytotoxic agents receivers. However, multivariate analysis revealed that only hematologic malignancy, infections acquired while hospitalized and previous use of parenteral antibiotics were risk factors for *P. aeruginosa* bacteremia.

Key word : *Pseudomonas aeruginosa* Bacteremia, Risk Factor

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Pseudomonas aeruginosa accounted for 6 per cent of bacteria isolated from blood samples taken from patients at Siriraj Hospital during 1998 and this organism was one of the most common bacteria causing nosocomial infections in Thailand[1]. The incidence of *P. aeruginosa* infections is on the increase due to increasing numbers of immunocompromised patients and advances in therapy of chronic and malignant diseases. Antibiotic therapy for *P. aeruginosa* infections is quite expensive and the case fatality rate is high[2-4]. Over the past decade, there have been attempts to prevent or minimize the risk of acquiring *P. aeruginosa* infections using measures to prevent and control nosocomial infections and improving the host defense mechanisms of the patients at risk. Immunoprophylaxis against *P. aeruginosa* infections has been proposed and a vaccine has been developed with promising results in the early phases [5-8]. Clinical trials on the efficacy of *P. aeruginosa* vaccine are being planned. In order to identify patients suitable for the *P. aeruginosa* vaccine trial, the objective of the study was to determine the risk factors of *P. aeruginosa* bacteremia in Thai patients.

PATIENTS AND METHOD

This was a case-control study conducted in patients admitted to Siriraj Hospital in 1998. The "case" group was patients with documented *P. aeruginosa* bacteremia. There were three "control" groups. Group 1 was patients with documented *Escherichia coli* bacteremia. Group 2 was patients with documented *Staphylococcus aureus* bacteremia. Group 3 was patients in whom blood cultures were performed but they revealed no organisms in their blood samples. A sample size of at least 65 patients per group was calculated from the following estimations. The risk factor in the case group was 60 per cent, odds ratio (OR) was 4, type I error was 5 per cent and type II error was 10 per cent. The demographics and potential risk factors i.e. type of infections, associated diseases/conditions, procedures/surgery, previous/current use of antibiotics and previous/current use of immunosuppressive agents were retrieved from the patients' medical records. Moreover, information on the site of infections, clinical features, antibiotic treatment and the outcome in patients with *P. aeruginosa* bacteremia were also collected. The data were analyzed by descriptive statistics, analysis of variance, non-parametric tests and multivariate analysis as appropriate. All comparisons were 2-sided and $p<0.05$ was considered statistically significant.

RESULTS

Out of 65 patients with *P. aeruginosa* bacteremia, 49 per cent were males and the mean age was 33 years. Ninety per cent of the patients had underlying diseases or conditions. Eighty-six per cent of the patients acquired infections while staying in the hospital. The common sites of infection were bacteremia (34%), skin and skin structure (28%), respiratory tract (26%) and urinary tract (14%). Fever and hypotension were prominent clinical features. Appropriate antibiotics were given to 94 per cent of the patients. The case fatality rate due to *P. aeruginosa* infection was 46 per cent. The comparative data among the 4 groups of patients are shown in Table 1. Univariate analyses revealed that the factors associated with *P. aeruginosa* bacteremia were nosocomial infections (OR 6.5, 95% CI 3-13.7), hematologic malignancy (OR 5.2, 95% CI 2.7-9.8), neutropenia (OR 4.8, 95% CI 2.5-9.1), COPD (OR 5.3, 95% CI 1.2-22.7), antibiotics (OR 3.9, 95% CI 2.1-7.1), parenteral antibiotics (OR 4.2, 95% CI 2.3-7.6) and cytotoxic agents (OR 3.4, 95% CI 1.8-6.2). However, multivariate analysis revealed that only hematologic malignancy, previous use of parenteral antibiotics and nosocomial infections were risk factors for *P. aeruginosa* bacteremia. The case fatality rates due to bacteremia in patients with *P. aeruginosa* bacteremia, *E. coli* bacteremia, *S. aureus* (MSSA) bacteremia and *S. aureus* (MRSA) bacteremia were 46 per cent, 30 per cent, 31 per cent, 53 per cent respectively ($p=0.02$).

DISCUSSION

The clinical features and clinical outcomes of the patients with *P. aeruginosa* bacteremia in the present study were not significantly different from other series [2-4]. This observation indicates that *P. aeruginosa* bacteremia in Thai patients is also serious and difficult to treat. The data in Table 1 indicated that *P. aeruginosa* bacteremia is common in the patients with hematologic malignancy, neutropenia, nosocomial infections, prior exposure to antibiotics and cytotoxic agents, and patients with unknown source of infections. In contrast, *E. coli* bacteremia was found in patients who had urinary tract infections and gastrointestinal infections and in patients with cirrhosis, whereas, *S. aureus* bacteremia was observed in patients who had intravascular devices and those with skin and skin structure infections. These findings are logical in the sense that *E. coli* reside in the gastrointestinal tract, whereas, *S. aureus* is usually

Table 1. Comparative data of the patients in 4 groups.

Character	*P. aeruginosa* bacteremia (N=65) %	*E. coli* bacteremia (N=65) %	*S. aureus* bacteremia (N=64) %	No bacteremia (N=65) %	P
Male	50	45	67	51	0.1
Mean age (years)	33	47	44	35	0.01
Nosocomial infections	86	47	58		<0.001
Neutropenia	42	17	11	11	<0.001
Hematologic malignancy	45	16	14	11	<0.001
Solid tumor	17	20	9	11	0.2
HIV/AIDS	5	9	11	3	0.2
Chronic Renal Failure	9	9	8	6	0.9
COPD	8	5	0	0	0.03
Congestive Heart Failure	14	11	14	6	0.5
Cirrhosis	2	13	3	2	0.01
Thalassemia	3	2	0	8	0.1
Prior use of antibiotics	69	36	34	40	<0.001
Cytotoxic agents	51	30	34	22	0.004
Surgery	22	9	11	22	0.1
Procedures	42	30	41	31	0.2
Endotracheal intubation	14	8	9	9	0.7
Intravenous devices	8	3	20	3	<0.001
Urinary catheter	19	19	22	17	0.2
Sites of Infections					
Respiratory	26	19	32		0.3
Urinary	14	39	8		<0.001
Gastrointestinal	8	28	3		<0.001
Skin	28	11	28		0.01
Undetermined	34	11	20		<0.001

colonized on the skin. Studies concerning risk factors for *P. aeruginosa* bacteremia have been reported[2, 3,9-12]. All of them are descriptive studies and they found advanced age, hematologic malignancy, neutropenia, diabetes mellitus, organ transplantation, severe burns, diffuse dermatitis, AIDS, corticosteroid therapy, antibiotic therapy, intravascular devices, surgery, trauma, urinary tract instrumentation and infections acquired while hospitalized were associated with *P. aeruginosa* bacteremia. The authors' descriptive results of patients with *P. aeruginosa* bacteremia also observed some of the aforementioned conditions. However, the present study attempted to identify risk factors by using a case control study design which is considered a more appropriate design for studying the risk factors. Three groups of control patients were used in order to be certain that the risk factors associated with *P. aeruginosa* bacteremia were really specific for *P. aeruginosa*. The authors found that only hematologic malignancy, previous use of parenteral antibiotics and nosocomial infections were risk factors for *P. aeruginosa* bacteremia in multivariate analysis. Therefore, Thai patients with hematologic malignancy should be the target population for interventions aimed to prevent *P. aeruginosa* bacteremia including *P. aeruginosa* vaccine.

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ปัจจัยเสี่ยงต่อภาวะติดเชื้อในกระแสเลือดจาก *Pseudomonas aeruginosa*†

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คณะผู้วิจัยได้ศึกษาปัจจัยที่เป็นปัจจัยเสี่ยงต่อการเกิดภาวะติดเชื้อในกระแสเลือดจาก *P. aeruginosa* ด้วยการวิจัยชนิด case control ในผู้ป่วยที่รับไว้รักษาในโรงพยาบาลศิริราชในปี พ.ศ. 2541 โดยกลุ่ม "case" คือผู้ป่วย 65 คนที่มีภาวะติดเชื้อในกระแสเลือดจาก *P. aeruginosa*, ส่วนกลุ่ม "control" มี 3 กลุ่ม ได้แก่ ผู้ป่วย 65 คนที่มีภาวะติดเชื้อในกระแสเลือดจาก *E. coli*, ผู้ป่วย 64 คนที่มีภาวะติดเชื้อในกระแสเลือดจาก *S. aureus* และผู้ป่วย 65 คนที่ไม่มีภาวะติดเชื้อในกระแสเลือด ผลการศึกษาพบว่าโรคมะเร็งของเม็ดเลือดขาว การติดเชื้อที่เกิดขึ้นในระยะที่ผู้ป่วยอยู่ในโรงพยาบาล และการได้รับยาต้านจุลชีพชนิดฉีดมาก่อนเป็นปัจจัยเสี่ยงต่อภาวะติดเชื้อในกระแสเลือดจาก *P. aeruginosa*

คำสำคัญ : ปัจจัยเสี่ยง, ภาวะติดเชื้อในกระแสเลือด

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