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Acute respiratory failure due to Pneumocystis pneumonia: outcome and prognostic factors

Viboon Boonsarngsuk*, Supinda Sirilak, Sumalee Kiatboonsri

Division of Pulmonary and Critical Care Medicine, Department of Medicine, Faculty of Medicine, Ramathibodi Hospital, Mahidol University, Bangkok 10400, Thailand

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KEYWORDS

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Prognostic factors;
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Positive end-expiratory pressure;
Mortality

Summary

Objectives: To examine the outcome and prognostic factors of in-hospital mortality in patients with acute respiratory failure (ARF) caused by Pneumocystis pneumonia (PCP) admitted to a medical intensive care unit.

Methods: A retrospective review was conducted of all patients with ARF from PCP in Ramathibodi Hospital between 2000 and 2006. Patient characteristics, clinical presentation, and laboratory, radiological and microbiological findings, as well as therapy and clinical course were included in the analysis of prognostic factors of death.

Results: A total of 14 HIV-infected and 30 otherwise immunosuppressed patients were identified. The overall mortality rate was 63.6%. Logistic regression analysis demonstrated that APACHE II score on day 1 and level of PEEP used on day 3 of respiratory failure were associated with higher hospital mortality. In a comparison between the HIV group and the non-HIV group, the early mortality rate was significantly higher in the HIV group, but late hospital mortality was not different between the two groups. Using a univariate logistic regression model, four parameters were found to be significantly associated with death in the HIV group: sex, APACHE II score on day 1, CMV co-infection, and level of PEEP on day 3 of ARF. In the non-HIV group, corticosteroid use prior to diagnosis of PCP and level of PEEP on day 3 of ARF were found to be the significant parameters.

Conclusion: The mortality rate in patients with ARF caused by PCP was high. Various variable factors were related to a poor prognosis. For improved survival, multimodality treatments are needed to reduce these risk factors.

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Introduction

Pneumocystis pneumonia (PCP), the disease caused by *Pneumocystis jirovecii*, emerged as an important cause of morbidity and mortality in HIV-infected patients from early in the AIDS epidemic.^{1,2} Currently, with the use of highly active

* Corresponding author. Tel.: +66 2 201 1619.
E-mail address: bss-vb@hotmail.com (V. Boonsarngsuk).

antiretroviral therapy (HAART), the prescription of prophylactic agents to persons at high clinical risk,³ and the availability of more sensitive immunofluorescence methods of *P. jirovecii* detection,⁴ the overall incidence of PCP cases and survival following PCP in AIDS patients has generally improved.⁵ In spite of this, the high mortality of patients requiring mechanical ventilation (MV) has remained unchanged, ranging from 50% to 60%.⁶

In contrast to AIDS-related cases, cases of PCP in patients with other predisposing immunodeficiency states, such as organ transplant recipients, patients with hematologic and solid tumors receiving chemotherapeutic agents, and persons with chronic inflammatory diseases requiring prolonged use of corticosteroids, may be increasing,⁷ and the associated mortality may be >50%.^{7,8} However, the previous literature on both HIV- and non-HIV-related PCP has indicated that the mortality of patients with acute respiratory failure (ARF) requiring MV does not differ widely and ranges between 40% and 60%, despite the use of new aggressive supportive interventions and monitoring.^{6,9–12}

In order to examine the outcome and prognostic factors of in-hospital mortality in patients with ARF requiring MV caused by PCP at our institution, we retrospectively collected data for PCP patients requiring MV and admitted to a medical intensive care unit (ICU) between 2000 and 2006. Clinical, laboratory, and radiologic features, as well as mechanical ventilation parameters were examined as prognostic factors of patient outcome.

Materials and methods

Subjects

We performed a retrospective analysis on all consecutive patients ≥ 15 years of age with a microbiologically confirmed diagnosis of PCP, who were admitted to the medical ICU of Ramathibodi Hospital, a tertiary university referral hospital in Bangkok, Thailand, and required treatment for ARF with MV between January 1, 2000 and November 30, 2006. All cases of PCP included in the study had cytologic documentation of the organisms by immunofluorescence or Giemsa staining in specimens of bronchoalveolar lavage (BAL) fluid or transbronchial biopsy (TBBX) specimens. Cases of presumptive diagnosis of PCP were not included. The study protocol was approved by the Ethics Committee on Human Experimentation of Ramathibodi Hospital, Faculty of Medicine, Mahidol University.

Data collection

Clinical data abstracted included the following: general demographic information, HIV status, underlying immunosuppressive condition, including medications and PCP prophylaxis, laboratory analysis, radiology, microbiology, APACHE (acute physiology and chronic health evaluation) II score on the day of ARF, mechanical ventilation parameters, antibiotic and steroid therapy, and hospital and ICU length of stay (LOS), as well as overall hospital mortality.

In our ICU, to ventilate any patient who developed acute respiratory failure with diffuse bilateral lung diseases, we routinely used a tidal volume of 8–10 ml per kilogram of

predicted body weight and optimal positive end-expiratory pressure (PEEP) by lung mechanics as described by Suter et al.¹³ With this technique, the PEEP was increased sequentially with a consistent tidal volume, and the static compliance was measured at each interval. Optimal PEEP, defined as the level of PEEP corresponding to maximal compliance, was chosen. The level of optimal PEEP was titrated once daily and recorded for three consecutive days. A plateau pressure of ≤ 30 – 35 cmH₂O was allowed.

Statistical analysis

All values were expressed as the mean \pm standard deviation (SD) for continuous variables and percent for categorical variables. To determine the association of independent variables with hospital mortality, continuous variables were compared using the Student's two-tailed *t*-test or nonparametric Mann–Whitney U-test, in case of distribution not being normal. The Chi-square test or the Fisher's exact test, in case of low expected frequencies, was used for comparisons of categorical variables. Variables identified as significant in the univariate analysis were assessed as predictors of mortality using logistic regression analysis. Then, subgroup analysis in both the HIV group and non-HIV-related PCP group was performed to find the prognostic factors associated with hospital mortality in the same manner. In-hospital survival was assessed by Kaplan–Meier methods, and differences between the HIV group and the non-HIV-related PCP group were assessed by the log-rank test. All statistical tests were two-sided, and $p < 0.05$ was considered statistically significant. All data were analyzed with a statistical software package (SPSS, version 11.5 for Windows; SPSS Inc., Chicago, IL, USA).

Results

Demographic features

A total of 44 confirmed cases of PCP in adult patients who developed ARF and required treatment with MV were identified during the period between January 1, 2000 and November 30, 2006. PCP was diagnosed by BAL in 41 out of 44 patients, while 13 cases were diagnosed by TBBX. Fourteen cases were HIV-seropositive and 30 cases had other conditions associated with immunosuppression. Of these 44 patients, 27 were female. The mean age of the patients was 46.3 years. The mean APACHE II score on day 1 was 22.3 (Table 1). The mean ICU and hospital LOS were 18 days and 25 days, respectively.

Immunosuppressive conditions

In the HIV group, seven (50%) were female and the mean age was 35.2 years. Of the 14 patients, 10 had been tested for CD4 count and the mean result was 53.1 cells/ μ l. Only one case had received trimethoprim/sulfamethoxazole (TMP/SMZ) prophylaxis.

In the non-HIV group, 20 (66.7%) were female and the mean age was 51.5 years. The underlying diseases of the conditions associated with immunosuppression are presented in Table 1. Eight patients had received systemic corticosteroids only. Two patients were treated with cytotoxic che-

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