Concurrent Bacterial Lung Infection in Patients with AIDS, PCP, and Respiratory Failure*

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Study Objectives: To determine and compare the incidence of concurrent bacterial lung infection in intubated and nonintubated patients with the acquired immunodeficiency syndrome (AIDS) and Pneumocystis carinii pneumonia (PCP) requiring medical intensive care unit (MICU) admission for support of their respiratory function.

Design: A retrospective review of medical records.

Setting: A large university hospital and AIDS treatment center.

Patients: All AIDS/PCP patients admitted to the MICU for support of oxygenation and/or ventilation between 1985 and 1989. Survival was defined as discharge from the hospital; nonsurvival was defined as death any time during the hospitalization. Patients with acute spinal cord injury (SCI) were used as controls to determine the incidence of nosocomial pneumonia in ICU patients of similar age without AIDS.

Measurements and Results: Twenty-nine AIDS/PCP patients met study criteria; eight (28 percent) were survivors and 21 (72 percent) were nonsurvivors. There was no significant difference in duration of intubation or duration of ICU stay between survivors and nonsurvivors with or without intubation. The incidence of bacterial concurrent lung infection (CLI) in AIDS/PCP patients overall was 7 percent and in intubated AIDS/PCP patients it was 10 percent. There was no statistically significant difference in the incidence of bacterial CLI between the survivors and nonsurvivors or between intubated and nonintubated patients with AIDS/PCP. The incidence of nosocomial pneumonia in SCI overall was 17 percent and in intubated SCI patients it was 30 percent.

Conclusions: The incidence of bacterial lung infections in our retrospective study of AIDS patients with PCP is remarkably less than in the general ICU population with respiratory failure and in our control patients with SCI, although the differences did not attain statistical significance. This finding may be related to antimicrobial therapy directed against P carinii. Endotracheal intubation in patients with AIDS and PCP, who were undergoing appropriate antimicrobial therapy, did not result in a significantly higher incidence of bacterial lung infections than in those who were not intubated. There was no significant difference in the incidence of bacterial lung infections between those AIDS/PCP patients who survived episodes of severe respiratory failure and those who did not. Endotracheal intubation should not be delayed or withheld from this patient population due to concerns of pulmonary bacterial superinfection.

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CLI = concurrent lung infection; CMV = cytomegalovirus; CPAP = continuous positive airway pressure; DFMO = difluoromethylornithine; MICU = medical intensive care unit; MRSCICU = Midwest Regional Spinal Cord Injury Care System; PPV = positive pressure ventilation; SCI = spinal cord injury; TMP/SMX = trimethoprim/sulfamethoxazole

The acquired immunodeficiency syndrome (AIDS) has been associated with an increased susceptibility to fulminant bacterial pneumonias1-3 and it has been reported at autopsy that the majority of AIDS patients with respiratory failure have concurrent bacterial bronchitis or bronchopneumonia.4 Since tracheal intubation is known to rapidly establish bacterial colonization of the tracheobronchial tree5 and to predispose patients to nosocomial pneumonia,4 the question arises as to whether tracheal intubation, in these immunocompromised patients, increases morbidity and mortality due to pulmonary bacterial superinfections. Since such an association could influence clinical judgments regarding tracheal intubation in patients with AIDS and Pneumocystis carinii pneumonia (PCP), we retrospectively investigated the incidence of bacterial concurrent lung infection (CLI) in AIDS/PCP patients requiring support of oxygenation and/or ventilation, with and without endotracheal intubation, in our medical intensive care unit (MICU). To provide a control group of ICU patients from our institution who were of similar age, we compared the incidence of nosocomial pneumonia in intubated AIDS/PCP patients with intubated spinal cord injury (SCI) patients.

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METHODS

AIDS/PCP Patients

The medical records of all patients with AIDS and PCP who were admitted to the MICU for support of oxygenation and/or ventilation between January 1, 1985 and March 31, 1989 were retrospectively reviewed. The study was approved by the Northwestern University Medical School (Chicago, Ill) Institutional Review Board. All patients treated by the Infectious Disease Service and Respiratory/Critical Care Service were divided into groups based on survival and endotracheal intubation. Survival was defined as discharge from the hospital; nonsurvival was defined as death at any time during the hospitalization.

Diagnosis

PCP was diagnosed in all patients by sputum induction with 3 percent saline solution or bronchoalveolar lavage (BAL). BAL was performed if P carinii organisms could not be identified on two consecutive induced sputum samples. Examination for P carinii organisms was carried out with Gomori's methenamine silver, toluidine blue-0, and Giema stains.

Sputum and BAL samples were also evaluated for the presence of bacterial, viral, fungal, and acid-fast organisms. Although controversy exists regarding the sensitivity and specificity of this procedure, most microscopic examination with Gram stain and cultures of sputum were performed with each acute febrile episode (temperature >38.6°C). Sputum samples with ≥10 epithelial cells or ≤25 neutrophils under high-power field were considered contaminated with oropharyngeal flora and not suitable for further examination. BAL fluid was considered inadequate for microbiologic evaluation if alveolar macrophages were identified in the specimen. Chest roentgenograms were evaluated for new focal infiltrates on a daily basis during the ICU course.

Concurrent lung infection was considered to be present if there was clinical evidence of a new infection (increasing fever, increasing WBC, new areas of lung consolidation on roentgenograms) in conjunction with the identification of predominant and intracellular bacterial organisms on Gram stain of the sputum. Sputum cultures and sensitivity testing were used to guide antibiotic therapy. In addition to the above clinical criteria, the diagnosis of CLI was made when a BAL sample demonstrated <1 percent squamous epithelial cells and >10⁶ colony-forming units of an organism/per milliliter. Although viral cultures were obtained on sputum samples, the diagnosis of viral lung infection required the presence of invasive viral inclusion bodies on histologic examination.

Blood cultures and urine Gram stains and cultures were also obtained with each acute febrile episode.

Antimicrobial Therapy

Antimicrobial therapy for PCP was determined by the Infectious Disease service. Initial treatment was with intravenous (IV) trimethoprim/sulfamethoxazole (TMP/SMX), 20 mg/kg/day TMP and 100 mg/kg/day SMX in divided doses. Patients who failed to respond (ie, improved oxygenation, defervescence, decreased dyspnea) within five to seven days and those demonstrating drug intolerance (leukopenia, thrombocytopenia, drug fever, hepatitis, or severe rash) were changed to IV pentamidine (4 mg/kg/day) therapy. Patients who did not respond (as with TMP/SMX) within five to seven days of pentamidine therapy or were intolerant of the drug (thrombocytopenia, hypoglycemia, hypotension, leukopenia, renal impairment, or pancreatitis), were considered for National Institutes of Health experimental protocols with trimetrexate or compassionate use of difluoromethylornithine (DFMO).

Antibiotic therapy for bacteria was based initially on the results of sputum Gram stains. Appropriate changes were initiated when sputum cultures and sensitivity testing were available. If neither microscopic sputum examination nor culture results were diagnostic, empiric antibiotic therapy was administered when concurrent bacterial pulmonary infection was suspected.

Airway Pressure Therapy

Methods of oxygenation and ventilatory support were determined by the Respiratory/Critical Care Service. When 50 percent inspired oxygen, administered by a high-flow analyzed oxygen delivery system, failed to maintain the arterial PaO₂ above 60 mm Hg, continuous positive airway pressure (CPAP) by face mask was the initial method of airway pressure therapy. Tracheal intubation was performed only if (1) an inadequate mask seal prevented CPAP maintenance, (2) the patient could not tolerate the CPAP mask, or (3) positive pressure ventilation (PPV) was required to relieve detrimental work of breathing or respiratory acidemia.

SCI Patients

In order to provide a control group with which to compare the incidence of nosocomial bacterial pneumonia in intubated non-AIDS ICU patients at our institution, we evaluated the frequency of nosocomial pneumonia in patients with acute SCI who were admitted to the Midwest Regional Spinal Cord Injury Care System (MRSCICS) from 1988 to 1989. Patients with acute SCI were chosen as a control group because they had a low incidence of preexisting lung disease, they were of similar age, and they were cared for by the same Respiratory and Critical Care physician group that cared for the AIDS/PCP patients. Information pertaining to the occurrence of infection was collected from the database of the MRSCICS. The diagnosis of nosocomial pneumonia was based on the same clinical criteria outlined above for AIDS/PCP patients.

Statistical Analysis

Age, duration of intubation, and duration of ICU stay were compared between groups using two-sample Student's t-tests and the Wilcoxon rank sum test. The distribution of bacterial CLIs and nosocomial pneumonias between groups was compared using Fisher's exact test (two-tailed) or χ² tests. A p value <0.05 was considered to be statistically significant.

RESULTS

AIDS/PCP Patients

Twenty-nine male patients met study criteria; eight (28 percent) were survivors and 21 (72 percent) were nonsurvivors. The mean ages of the survivors and nonsurvivors were 32.8 ± 7.9 years and 37.0 ± 10.4 years. The mean days of intubation were 4 ± 5 (1-21) days or <0.05 days (NI-NS). There were significant differences between the groups in the number of days of intubation, as shown in Table 1.
years (p = 0.27), respectively.

Four of the nine patients who were not intubated met criteria for intubation but refused the procedure; all four died. One nonsurvivor was intubated during cardiopulmonary resuscitation but did not respond to the resuscitative efforts; therefore, he was classified as nonsurviving. The four survivors who did not require intubation were supported with CPAP by face mask during their ICU course. There was no significant difference in the mean duration of intubation (survivors: 4.6 ± 3.1 days; nonsurvivors: 10.5 ± 12.0 days; p = 0.1) or the mean duration of ICU stay between survivors and nonsurvivors with or without intubation (Fig 1).

Table 1 outlines CLI and antimicrobial therapy as related to intubation and survival. There was no significant difference in the incidence of bacterial CLI between the survivors and nonsurvivors or between intubated and nonintubated patients. In addition to the cytomegalovirus (CMV) infections noted in Table 1, one intubated survivor and three intubated nonsurvivors had sputum cultures positive for CMV; however, none of these three nonsurvivors demonstrated viral tissue invasion on histologic examination. The survivor did not undergo a lung biopsy, but did not have a clinical picture considered to be consistent with CMV pneumonitis. Therefore, these patients were not classified as having a CLI with CMV.

The duration of broad-spectrum antibiotic therapy prior to intubation was not significantly different between survivors and nonsurvivors (intubated survivors: 2.0 ± 2.2 days; intubated nonsurvivors: 4.9 ± 4.2 days; p = 0.09). Only one patient received prophylactic aerosolized pentamidine for PCP. Autopsies were obtained in ten of the nonsurvivors, eight of whom had been intubated. In only one patient, with Gram-negative bronchopneumonia, was the postmortem diagnosis of pulmonary infection different from the premortem clinical diagnosis. All autopsied patients demonstrated diffuse, severe consolidation of all lung regions and alveolar filling with foamy exudates and inflammatory cells. Active interstitial fibrosis, interstitial edema, and diffuse alveolar damage were also noted in the majority of autopsy results.
Table 2—Incidence of Nosocomial Pneumonia in AIDS/PCP and SCI Patients*

<table>
<thead>
<tr>
<th>Patients</th>
<th>Nosocomial Pneumonia</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>AIDS/PCP overall</td>
<td>7% (2/29)</td>
<td>&lt;0.17</td>
</tr>
<tr>
<td>SCI overall</td>
<td>17% (47/282)</td>
<td></td>
</tr>
<tr>
<td>AIDS/PCP intubated</td>
<td>10% (2/20)</td>
<td>&lt;0.08</td>
</tr>
<tr>
<td>SCI intubated</td>
<td>30% (19/63)</td>
<td></td>
</tr>
</tbody>
</table>

*AIDS = acquired immunodeficiency syndrome; PCP = Pneumocystis carinii pneumonia; SCI = spinal cord injury.

SCI Patients

Of the 282 patients admitted to the spinal cord ICU between 1988 and 1989, 225 (80 percent) were male and 57 (20 percent) were female. The mean age of the overall SCI patient population was 36.7 ± 17.6 years. The overall incidence of nosocomial pneumonia in the SCI population was 47/282 (17 percent).

Sixty-three patients (49 male [78 percent] and 14 female [22 percent]) required intubation for airway protection (seven [11 percent]), mechanical ventilation (51 [81 percent]), bronchial hygiene (19 [30 percent]), or airway obstruction (five [8 percent]). The mean age of the SCI patients who were intubated was 39.3 ± 20.7 years. Nineteen (30 percent) of the intubated SCI patients developed pneumonia ≥48 h after intubation. None of the patients requiring intubation had preexisting lung disease and only 11 (18 percent) of the 63 had concurrent chest trauma (pulmonary contusion, myocardial contusion, diaphragmatic injury, rib fractures, pneumothorax, and/or hemothorax). Table 2 outlines the incidence of bacterial nosocomial pneumonia in the various AIDS/PCP and SCI groups.

DISCUSSION

Human immunodeficiency virus type 1 (HIV 1) infection results in depletion of T lymphocytes and a decrease in the ratio of T-helper to T-suppressor (CD4/CD8) cells.13 There is also evidence that B-lymphocyte function is abnormal in these patients.14 These quantitative and qualitative immunologic defects predispose this patient population to infections with both common and opportunistic pathogens. Despite these immunologic abnormalities, the 7 percent (2/29) overall incidence of bacterial CLI that we report in the AIDS/PCP patient population is remarkably less than the 24 percent incidence of nosocomial pneumonia reported in the general ICU population requiring mechanical ventilation14 and the 17 percent overall incidence of nosocomial pneumonia we noted in patients admitted to our spinal cord ICU. Also, this is contrary to previous reports of higher incidences of bacterial lung infections concurrent with PCP.14 If only the intubated PCP patients are considered, the incidence of bacterial CLI still remains surprisingly low at 10 percent (2/20) as compared with the 30 percent incidence noted in intubated SCI patients. Although the differences between intubated AIDS/PCP patients and intubated SCI patients only approached statistical significance (Table 2), the trend is clear and may have proved significant if a larger AIDS/PCP patient population were available.

The incidence of bacterial CLI was not different between the intubated and nonintubated AIDS/PCP patients or between the AIDS/PCP survivors and nonsurvivors, and was much lower than the SCI control group. Thus, endotracheal intubation does not appear to adversely affect morbidity or mortality in this patient population in relation to bacterial superinfection.

Based on these findings, it seems that even these severely compromised AIDS patients retain sufficient immunologic function to combat bacterial lung infections in the face of appropriate antibacterial therapy. In addition, the particularly low incidence of bacterial CLI noted in this patient population may be related to the fact that the drug of first choice for PCP, TMP/SMX, also carries broad-spectrum activity against Gram-positive and Gram-negative bacteria.

CONCLUSIONS

The incidence of bacterial lung infections in our retrospective study of AIDS patients with PCP is remarkably less than in the general ICU population with respiratory failure and our control group of SCI patients. This finding may be related to the type and timing of antimicrobial therapy directed against P. carinii. Endotracheal intubation in patients with AIDS and PCP, who are undergoing appropriate antimicrobial therapy, does not result in a significantly higher incidence of bacterial lung infections than in non-AIDS patients or in those AIDS/PCP patients who are not intubated. There is no significant difference in the incidence of bacterial lung infections between those AIDS/PCP patients who survive episodes of severe respiratory failure and those who do not. Endotracheal intubation should not be delayed or withheld from AIDS/PCP patients due to concerns of pulmonary bacterial superinfection.

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REFERENCES

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