Pneumonia Following Closed Head Injury¹-⁴

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Introduction

Hospital-acquired pneumonia (HAP) is common among intubated patients (1, 2). Numerous studies have shown that airway colonization with bacteria, typically gram-negative rods, usually takes place within 2 to 3 days after endotracheal intubation, followed by development of clinical infection 3 to 7 days later (3-5). Studies establishing the risk factors, pathogenesis, and clinical characteristics of HAP have mainly involved patients with serious underlying medical conditions, or they have included individuals with a wide spectrum of primary diagnoses (1, 6, 7).

Closed head injury (CHI) is a common condition requiring endotracheal intubation and mechanical ventilation in hospitals dealing with trauma, and might represent a different clinical setting with respect to the pathogenesis of pneumonia. In patients with CHI who are comatose when first seen in the field, initial aspiration of oropharyngeal contents might constitute a separate risk factor for development of pneumonia, in addition to later lower airway colonization following intubation. If this were the case, clinical pneumonia might be more common during the first few days of hospitalization in these patients than in those with other illnesses requiring intubation. Alternatively, patients with isolated CHI might be at less risk for pneumonia than those previously studied because of the absence of concomitant injury or underlying medical illness.

Prognosis for full recovery following CHI is largely determined by the severity of injury, the most commonly used measure of which is the Glasgow coma score (GCS) (8, 9).

We studied a large consecutive series of patients with isolated severe CHI in order to determine the incidence of pneumonia in this distinct population, to determine at what stage pneumonia developed in such individuals, and to determine whether injury severity, as reflected in the GCS, is an additional risk factor for pneumonia in patients who require endotracheal intubation and mechanical ventilation.

Methods

We reviewed 429 consecutive admissions of CHI to Harborview Medical Center, a 330-bed trauma center, for the years 1987 and 1988. Patients were identified from a trauma registry with confirmation of the list obtained from a separately maintained nosocomial infection registry. Fifteen charts of CHI patients identified by the registries could not be found. Patients were included only if their GCS on admission was ≤ 7T (or ≤ 8 if their trachea was not intubated at the time of arrival). All patients not yet intubated at the time of arrival were intubated in the emergency room. We excluded patients with chest injuries, abdominal injuries, or immobilizing skeletal injuries. We also excluded patients with a known history of respiratory disease and children under 1 yr of age as well as patients who had infiltrates present on the emergency room chest roentgenogram.

Pneumonia was defined using the following criteria: a new or progressing pulmonary infiltrate on chest roentgenograms plus two of the following three clinical or laboratory findings—(1) new fever > 38.5°C rectally; (2) peripheral white blood count > 12,000/mm³; (3) new purulent tracheobronchial secretions. These criteria are minimally modified from the studies of nosocomial pneumonia by Celis and colleagues (2) and Torres and coworkers (10). Our criteria differed only in requiring a fever of > 38.5°C rather than 38°C and a leukocyte count of > 12,000/mm³ rather than > 10,000/mm³. In addition, any alternative explanation for the findings resulted in exclusion of the diagnosis of pneumonia.

All patients were treated according to Harborview Medical Center standard neurosurgical intensive care protocols. All patients with GCS ≤ 8 were routinely intubated. Patients were initially hyperventilated and an intracranial pressure (ICP) monitor placed. Hyperventilation, hyperventilation, hyperventilation, and elevation of the head of the bed were used to maintain ICP below 20 mm Hg and cerebral perfusion pressure above 50 mm Hg (11). Phenytoin was used to control seizures, and pancuronium paralysis was used when necessary.

SUMMARY Pneumonia is common among patients with artificial airways in place. Most prior studies of such pneumonia involve a heterogeneous group of patients, usually with major medical or surgical illnesses. We studied the incidence of pneumonia in a group of patients with isolated closed head injury (CHI) in an effort to determine the pattern of the problem in the absence of other injuries and to determine whether the pattern of development of pneumonia in these patients was comparable to that in more heterogeneous groups of mechanically ventilated patients. We studied 109 initially comatose patients with isolated CHI who were ventilated 24 h or more. The mean age was 30.3 ± 20.2 yr, 72% were male, and the admission Glasgow coma score was 4.9 ± 1.4. Overall, 45 patients (41%) developed pneumonia, with the majority (29/45) occurring during the first 3 days of hospitalization. No patient developed pneumonia after the first week despite the fact that many were still ventilated, others remained intubated, and yet others were extubated but comatose. Patients who developed pneumonia experienced a longer ICU stay (10.5 ± 5.4 days versus 7.2 ± 4.3 days, p = 0.001) and hospital stay (34.8 ± 27.6 versus 22.5 ± 20.2 days, p = 0.01). We concluded that (1) CHI is associated with a high incidence of pneumonia; (2) pneumonia occurs earlier in CHI than in other patient groups, suggesting that the etiology may be different; (3) pneumonia does not tend to occur after the first week of hospitalization in CHI; (4) extubation of CHI patients did not tend to lead to pneumonia; and (5) pneumonia prolongs ICU and hospital stay in CHI patients.

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cicular activity increased ICP or made ventila-

tion difficult.

Patients were ventilated via either an or­

totracheal, nasotracheal or trans-tracheally

placed artificial airway. Cuffs were checked

at least once every 8 h to ensure pressures of

< 30 cm H2O. The ventilator circuit was rou­

tinely changed every 48 h. All patients had a

nasogastric tube in place for administration

of antacids, and an H2 blocker was adminis­

tered routinely (7, 12). Daily roentgeno­

grams and peripheral white blood counts were

performed.

Criteria for cessation of mechanical venti­

lation included: ICP < 20 mm Hg during

spontaneous ventilation and the ability to

maintain a PaO2 > 70 mm Hg on an Fio2 <

0.4 and CPAP < 5 cm H2O. Criteria for extu­

bation of the trachea included independence

from mechanical ventilation, intact cough, and a

gag reflex. In the absence of a cough or gag reflex

follow ing weaning from mechanical ventila­

tion, a tracheotomy was performed. Five patients

underwent tracheotomy on the day of the initial

injury because of concomitant facial injuries.

Antibiotic therapy varied depending on the

primary attending physician, but included ini­

tiation of therapy with broad spectrum cover­

age using two drugs whose sensitivity includ­

ed the prevalent Pseudomonas species in this

institution, with subsequent narrowing of the

spectrum based on sputum culture.

Statistical Methods

All means are reported with standard devia­

tions. Means were compared using Student's

t test for two independent samples. The chi­

square statistic was used to compare propor­

tions. Tests for homogeneity and linear trend

(13) based on the chi-square statistic were used

when three or more proportions were consid­

ered at one time. In order to ascertain the re­

lative effects of mechanical ventilation, tra­

cheal intubation, and extubation on the inci­

dence of pneumonia, estimates of relative risk

with 95% confidence intervals were obtained

using Cox's proportional hazards model (14)

with time-dependent co-variates.

Results

A total of 174 patients met the criteria for

isolated CHI and had artificial air­

ways in place. Of these, 31 patients died

within 24 h, and 34 were weaned from

ventilation in less than 24 h. This left 109

initially comatose patients with isolated

CHI who were ventilated 24 h or more

for data analysis. Mean age was 30.3 ±

20.2 yr, with a range of 1 to 88 yr, and

72% were male. The mean injury severi­

ty score (ISS) (15) on admission was 27.5

± 7.6, and the GCS was 4.9 ± 1.4 (table

1).

Figure 1 summarizes the clinical course of

respiratory support during the first

3 wk of hospitalization. The number of

patients requiring mechanical ventilation

(MV) decreased, while the number of pa­

tients remaining intubated but not ven­

tilated grew during the period shown.

Forty-five patients (41%) developed pneu­

monia. Forty-three of the 45 had purulent

sputum, with only 2 meeting the defini­
tion of pneumonia by chest X-ray, fever, and

leukocytosis alone. The mean age of patients

developing pneumonia was slightly greater than

of those who did not (34.6 versus 27.2) but

was only of marginal significance (p = 0.07).

Males predominated in those who developed

pneumonia out of proportion to their presence in

the study group, but the statistical significance

of this was also marginal (p = 0.06) (table 1).

Neither the admission ISS, the GCS on admission,

nor the GCS at 24 h was predictive of the patients

who later developed pneu­

monia (table 1). Further efforts to test

the relationship between different levels of

GCS on admission and the acquisition of

pneumonia using the trend test

(p = 1.0) and the homogeneity test (p = 0.55)

showed no correlation at all. Testing the

relationship of the GCS at 24 h with acquisition of pneumonia gave similar results; p = 0.17 for the homogeneity test and p = 0.65 for the linear trend test

(figure 2).

Mortality was 13% in pneumonia pa­

tients versus 22% in patients not develop­
ing pneumonia (p = 0.26) (table 2). How­

ever, both the duration of MV and the

duration of intubation were significantly

longer for patients who developed pneumonia

(8.2 ± 5.1 days versus 5.3 ± 4.3 days, p = 0.001 and 21.1 ± 24.6 days

versus 12.2 ± 16.8 days, p = 0.04, respec­


tively) (figure 2)
leagues (16) found that only one-third of the patients with the clinical syndrome in all cases. The study of Fagon and colleagues may not represent bacterial pneumonia and hospital stay in CHI patients. pneumonia may be different; and (5) pneumonia prolongs ICU stay in CHI patients did not tend to lead to pneumonia while in hospital. This compares with reported incidences of hospital acquired pneumonia in heterogeneous patient groups during MV (1, 7, 9, 17) ranging from 3.7% to 41%. Old age (>65 yr) (2, 6) as well as severe underlying conditions, i.e., shock, coma (6, 7), preexisting lung disease, and status postsurgery (2, 6, 18) were the common risk factors for the development of HAP in other series. Head injury patients developing pneumonia may well contain a mixture of patients whose pneumonia results from aspiration at the time of injury and those who develop true HAP. Depressed consciousness and large volume aspiration have been recognized as factors independently associated with nosocomial pneumonia (2). Clinically significant impairment of airway reflexes, i.e., delay in glottic closure, absence of cough reflex, and loss of spontaneous breathing in deep coma (19) carry risk of aspiration. At the onset of an acute illness, such as head trauma or a stroke, massive aspiration of oropharyngeal contents occurs before or during emergency treatment. Subsequent delay in clearance of bacterial contamination results in an early onset of pneumonia (defined as occurrence within 4 days of admission) (19–21). Such early onset was observed in 82% of total cases in our study population. Remarkably, only one of 34 patients extubated in less than 24 h developed pneumonia. Possible explanations for this include (1) rapid improvement permitted better pulmonary toilet and better coughing, (2) the absence of the endotracheal tube decreased the risk, and (3) selection bias in that patients who had any early signs of pneumonia were left intubated. The intubated CHI patients, while receiving MV either for hyperventilation to control ICP or because of respiratory failure, are at high risk for airway bac-

**TABLE 2**

<table>
<thead>
<tr>
<th>Whole Group</th>
<th>With Pneumonia</th>
<th>Without Pneumonia</th>
</tr>
</thead>
<tbody>
<tr>
<td>(n = 109)</td>
<td>(n = 45)</td>
<td>(n = 64)</td>
</tr>
<tr>
<td>Mortality (%)</td>
<td>0.01</td>
<td>0.001</td>
</tr>
<tr>
<td>Days ventilated</td>
<td>6.5 ± 4.9</td>
<td>8.2 ± 5.1</td>
</tr>
<tr>
<td>Days intubated</td>
<td>15.9 ± 20.8</td>
<td>21.1 ± 24.6</td>
</tr>
<tr>
<td>Days in ICU</td>
<td>8.6 ± 5.0</td>
<td>10.5 ± 5.4</td>
</tr>
<tr>
<td>Days in hospital</td>
<td>27.6 ± 24.2</td>
<td>34.8 ± 27.6</td>
</tr>
</tbody>
</table>

*Data expressed as mean ± SD.
†Probability of patients with pneumonia versus patients without pneumonia.

**TABLE 3**

<table>
<thead>
<tr>
<th>Hospital Day</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
<th>7</th>
<th>8</th>
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<tbody>
<tr>
<td>On ventilator</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>4/109</td>
<td>(4%)</td>
<td>9/100</td>
<td>15/78</td>
<td>5/43</td>
<td>1/30</td>
<td>1/22</td>
<td>1/17</td>
<td>0/13</td>
</tr>
<tr>
<td>Off ventilator</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>–</td>
<td>–</td>
<td>0/03</td>
<td>1/7</td>
<td>0/6</td>
<td>1/10</td>
<td>1/11</td>
<td>0/8</td>
<td></td>
</tr>
<tr>
<td>Still intubated</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>–</td>
<td>–</td>
<td>0/14</td>
<td>2/27</td>
<td>0/30</td>
<td>1/31</td>
<td>2/29</td>
<td>0/29</td>
<td>0/29</td>
</tr>
<tr>
<td>Exintubated</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>–</td>
<td>–</td>
<td>0/06</td>
<td>1/7</td>
<td>0/6</td>
<td>1/31</td>
<td>2/29</td>
<td>0/29</td>
<td>0/29</td>
</tr>
</tbody>
</table>

**TABLE 4**

<table>
<thead>
<tr>
<th>Severity</th>
<th>Days Ventilated</th>
<th>Days Intubated</th>
<th>Days in ICU</th>
</tr>
</thead>
<tbody>
<tr>
<td>GCS on admission</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 7.5, n = 68</td>
<td>7.6 ± 5.4</td>
<td>9.1 ± 14.9</td>
<td>9.5 ± 5.7</td>
</tr>
<tr>
<td>&gt; 7.0, n = 41</td>
<td>4.7 ± 3.1</td>
<td>9.2 ± 12.7</td>
<td>7.0 ± 3.3</td>
</tr>
<tr>
<td>GCS at 24 h</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>&lt; 7.5, n = 52</td>
<td>7.7 ± 5.3</td>
<td>22.0 ± 25.6</td>
<td>9.5 ± 5.8</td>
</tr>
<tr>
<td>&gt; 7.5, n = 47</td>
<td>4.6 ± 3.3</td>
<td>9.2 ± 12.7</td>
<td>8.9 ± 3.5</td>
</tr>
</tbody>
</table>

*Definition of abbreviation: HAP = hospital-acquired pneumonia.
* Numerator represents the number of patients in that category first diagnosed with HAP that day, while denominator represents total patients in that category who have not previously developed pneumonia.

**Discussion**

The important findings of this study are that (1) CHI is associated with a high incidence of pneumonia; (2) pneumonia occurs earlier in CHI than in other patient groups, suggesting that the etiology may be different; (3) pneumonia does not tend to occur after the first week of hospitalization in CHI; (4) extubation of CHI patients did not tend to lead to pneumonia; and (5) pneumonia prolongs ICU and hospital stay in CHI patients. Usually considered to be ventilator-associated pneumonia have positive cultures on quantitative protected brush specimens. Our study represents a study of the clinical syndrome of pneumonia, and future studies with more selective diagnostic techniques could reveal prognostic differences among subgroups.

We found that pneumonia is common (41% incidence) after severe CHI and occurs early during hospitalization. This compares with reported incidences of hospital acquired pneumonia in heterogeneous patient groups during MV (1, 7, 9, 17) ranging from 3.7% to 41%. Old age (>65 yr) (2, 6) as well as severe underlying conditions, i.e., shock, coma (6, 7), preexisting lung disease, and status postsurgery (2, 6, 18) were the common risk factors for the development of HAP in other series. Head injury patients developing pneumonia may well contain a few patients whose pneumonia results from aspiration at the time of injury and those who develop true HAP. Depressed consciousness and large volume aspiration have been recognized as factors independently associated with nosocomial pneumonia (2). Clinically significant impairment of airway reflexes, i.e., delay in glottic closure, absence of cough reflex, and loss of spontaneous breathing in deep coma (19) carry risk of aspiration. At the onset of an acute illness, such as head trauma or a stroke, massive aspiration of oropharyngeal contents occurs before or during emergency treatment. Subsequent delay in clearance of bacterial contamination results in an early onset of pneumonia (defined as occurrence within 4 days of admission) (19–21). Such early onset was observed in 82% of total cases in our study population. Remarkably, only one of 34 patients extubated in less than 24 h developed pneumonia. Possible explanations for this include (1) rapid improvement permitted better pulmonary toilet and better coughing, (2) the absence of the endotracheal tube decreased the risk, and (3) selection bias in that patients who had any early signs of pneumonia were left intubated. The intubated CHI patients, while receiving MV either for hyperventilation to control ICP or because of respiratory failure, are at high risk for airway bac-

**TABLE 2 OUTCOME DATA OF PATIENTS WITH ISOLATED CLOSED HEAD INJURY**

- Mortality (%): Whole Group (n = 109) = 0.01, With Pneumonia (n = 45) = 0.001, Without Pneumonia (n = 64) = 0.001
- Days ventilated: Whole Group = 6.5 ± 4.9, With Pneumonia = 8.2 ± 5.1, Without Pneumonia = 5.3 ± 4.3
- Days intubated: Whole Group = 15.9 ± 20.8, With Pneumonia = 21.1 ± 24.6, Without Pneumonia = 12.2 ± 16.8
- Days in ICU: Whole Group = 8.6 ± 5.0, With Pneumonia = 10.5 ± 5.4, Without Pneumonia = 7.2 ± 4.3
- Days in hospital: Whole Group = 27.6 ± 24.2, With Pneumonia = 34.8 ± 27.6, Without Pneumonia = 22.5 ± 20.2

*Data expressed as mean ± SD.
†Probability of patients with pneumonia versus patients without pneumonia.

**TABLE 3 DAILY INCIDENCE OF PNEUMONIA IN RELATION TO INTUBATION AND VENTILATION STATUS**

- Hospital Day 1: On ventilator 4/109, Off ventilator 0/03, Still intubated 0/14
- Hospital Day 2: On ventilator 9/100, Off ventilator 0/06, Still intubated 1/7, Extubated 0/06
- Hospital Day 3: On ventilator 15/78, Off ventilator 1/10, Still intubated 1/31, Extubated 1/31
- Hospital Day 4: On ventilator 5/43, Off ventilator 1/11, Still intubated 2/29, Extubated 2/29
- Hospital Day 5: On ventilator 1/30, Off ventilator 1/22, Still intubated 2/29, Extubated 2/29
- Hospital Day 6: On ventilator 1/22, Off ventilator 1/17, Still intubated 2/29, Extubated 2/29
- Hospital Day 7: On ventilator 1/17, Off ventilator 0/13, Still intubated 2/29, Extubated 2/29
- Hospital Day 8: On ventilator 0/13, Off ventilator 0/06, Still intubated 0/06, Extubated 0/06

*Definition of abbreviation: HAP = hospital-acquired pneumonia.
* Numerator represents the number of patients in that category first diagnosed with HAP that day, while denominator represents total patients in that category who have not previously developed pneumonia.

**TABLE 4 EFFECT OF INJURY SEVERITY ON DURATION OF RESPIRATORY ASSISTANCE AND LENGTH OF ICU STAY**

- GCS on admission
  - > 7.5, n = 68: 7.6 ± 5.4 days, p = 0.001
  - > 7.0, n = 41: 4.7 ± 3.1 days, p = 0.004
- GCS at 24 h
  - < 7.5, n = 52: 7.7 ± 5.3 days, p = 0.001
  - > 7.5, n = 47: 4.6 ± 3.3 days, p = 0.002

*Definition of abbreviation: GCS = Glasgow coma score.
* Data expressed as mean ± SD.
†GCS data not available on all patients at 24 h.
PNEUMONIA IN HEAD-INJURED PATIENTS

For all CHI patients, the duration of MV, the length of ICU stay, and the possibility of sustaining a prolonged course of intubation correlated with the initial GCS (table 4). This could not be accounted for by pneumonia, because acquisition of pneumonia bore no relationship with severity of injury. The extremely low admission GCS of 3.0 ± 0.2T in 31 patients excluded from the study, because they died within 24 h of admission, also confirms the predictive value of GCS.

The role of tracheotomy in the acquisition of nosocomial pneumonia remains undetermined. Cross and Roup (17) reported a 25% incidence (13/52) of HAP in patients who had a tracheostomy without MV for longer than 24 h, while Celis and colleagues (2) did not find that tracheostomy was an independent risk factor for the development of HAP pneumonia. In the present study, 37 patients (34%) with and without MV had a trans-tracheal airway placed for a mean duration of 8.9 ± 4.8 days. Twenty-one episodes of pneumonia developed in these patients, but all occurred before tracheotomy was performed. Another five patients had tracheotomy on the first day of admission, and none developed HAP.

The mean GCS upon discontinuation of ventilation for the entire group was 6.5 ± 2.2T (n = 86), indicating that a significant proportion of patients remained comatose at the time of ventilator weaning. Despite this, very few patients developed pneumonia following extubation. Thus, early extubation once mechanical ventilation is no longer needed does not appear to increase the risk of pneumonia, even in the severely head injured population.

Accurate diagnosis of bacterial pneumonia and isolation of the causative agent(s) in patients receiving MV are often difficult (1, 7, 24, 25). We recognize that even in comparable study populations, using different criteria for case definition results in different incidences of pneumonia. When feasible, specific diagnostic techniques such as protected specimen brush and transthoracic needle aspiration (6, 18) and autopsy (6, 18, 25, 26) findings are ideal. However, our use of accepted clinical criteria for identification of cases is practical and provides a standard procedure for making the diagnosis.

In a study of independent risk factors in all mechanically ventilated patients, Torres and coworkers (10) found that risk of pneumonia was increased by reintubation, gastric aspiration, a duration of mechanical ventilation of > 3 days, and underlying COPD. Patients in the last category were excluded in our group, as were patients with massive aspiration, because all our patients had a clear CXR on admission to the hospital. Our study contrasts with their study in that the greatest incidence of pneumonia in our series was early in the hospital course with no pneumonias occurring after the first week. This provides further evidence that isolated CHI may result in a very different pattern of pneumonia.

The study by Craven and coworkers (7) of risk factors for nosocomial pneumonia during mechanical ventilation found four variables—intracranial pressure monitoring, H2 blocker treatment, 24- versus 48-h ventilator circuit changes, and fall–winter season—significantly associated with pneumonia. All of our patients had ICP monitors in place and all were treated with H2 blockers, placing them into a high-risk category. Our patients' circuits were changed every 48 h, and we did not study seasonal variations in the incidence of pneumonia. In their study, head trauma patients had a crude odds ratio of 3.4 for developing pneumonia. However, the patients were not selected to have isolated CHI and, thus, could have had other risk factors. Unlike our patients, their head injury patients were treated with corticosteroids, which also might have increased risk. This study and our study agree that head-injured patients have a high risk of developing pneumonia. Our study further demonstrates that this is true even with isolated head injury, but that the risk is early and does not seem to be related to longer duration of ventilation.

Our review of pneumonia in this relatively homogeneous population demonstrates that this subpopulation of patients undergoing mechanical ventilation may differ substantially from previously reported populations. The incidence of pneumonia was high compared to that in other reports, and ended to occur early in the course and never occurred after the first week. This early occurrence is consistent with an increased risk of initial aspiration of oropharyngeal and/or gastric contents because of the associated loss of consciousness. The low incidence of pneumonia later in our patients' hospitalizations, as compared with other series, may reflect the fact that patients with isolated head injuries are otherwise healthy. Thus, intubation and mechanical ventilation may be relatively low risk in the absence of other injuries.

Finally, extubation of comatose pa-
tients appeared to be relatively low risk. This finding suggests that extubation can be carried out once an artificial airway is no longer needed for either hyperventilation or because of respiratory failure.

**Acknowledgment**

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**References**