Pneumonia Following Closed Head Injury[1–4]

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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 4.9T ± 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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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 Glascow 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 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, hyperosmotic agents, 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 mus-

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cular activity increased ICP or made ventilation difficult.

Patients were ventilated via either an orotracheal, nasotracheal or trans-tracheally placed artificial airway. Cuffs were checked at least once every 8 h to ensure pressures of < 30 cm H_2O. The ventilator circuit was routinely changed every 48 h. All patients had a nasogastric tube in place for administration of antacids, and an H2 blocker was administered routinely (7, 12). Daily roentgenograms and peripheral white blood counts were performed.

Criteria for cessation of mechanical ventilation included: ICP < 20 mm Hg during spontaneous ventilation and the ability to maintain a $Pa_{O_2} > 70$ mm Hg on an $FI_{O_2} \leqslant 0.4$ and CPAP $\leqslant$ 5 cm H_2O. Criteria for extubation of the trachea included independence from mechanical ventilation, intact cough, and a gag reflex. In the absence of a cough or gag reflex following weaning from mechanical ventilation, 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 initiation of therapy with broad spectrum coverage using two drugs whose sensitivity included 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 deviations. Means were compared using Student's *t* test for two independent samples. The chi-square statistic was used to compare proportions. Tests for homogeneity and linear trend (13) based on the chi-square statistic were used when three or more proportions were considered at one time. In order to ascertain the relative effects of mechanical ventilation, tracheal intubation, and extubation on the incidence 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 airways 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 severity score (ISS) (15) on admission was 27.5 ± 7.6, and the GCS was 4.9T ± 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 patients remaining intubated but not ventilated grew during the period shown.

Forty-five patients (41%) developed pneumonia. Forty-three of the 45 had purulent sputum, with only 2 meeting the definition 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 pneumonia (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 patients versus 22% in patients not developing pneumonia (p = 0.26) (table 2). However, 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-

TABLE 1

CLINICAL CHARACTERISTICS OF PATIENTS STUDIED*

	Total with CHI (*n* = *109*)	With HAP (*n* = *45*)	Without HAP (*n* = *64*)	p Value†
Mean age (range), yr	30.3 (1–88)	34.6 (3–88)	27.2 (1–85)	0.07
Sex (M/F)	79/30	37/8	42/22	0.056
Admission ISS	27.5 ± 7.6	27.5 ± 5.9	27.5 ± 8.5	0.99
GCS on admission	4.9 ± 1.4	4.8 ± 1.5	4.9 ± 1.4	0.91
GCS at 24 h	5.4 ± 1.8	5.3 ± 1.7	5.5 ± 1.9	0.55

Definition of abbreviations: CHI = closed head injury; HAP = hospital-acquired pneumonia; ISS = injury severity score; GCS = Glasgow coma score (all "T" omitted).

* Results are expressed as mean ± SD or number of patients.

† Probability of patients with HAP versus patients without HAP.

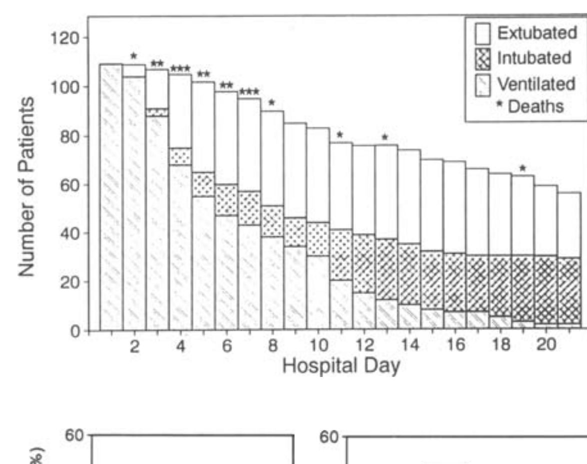

Fig. 1. Daily frequencies of the study population with regard to treatment with mechanical ventilation (*hatched area*), discontinuation of ventilation but retaining the tube (*crossed area*), or status postextubation (*open area*).

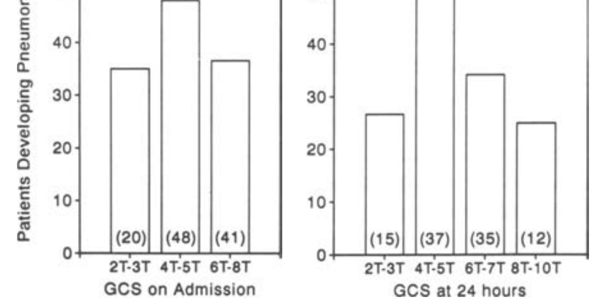

Fig. 2. Percentages of patients who developed pneumonia during hospitalization according to Glasgow coma score on admission (*left*) and at 24 h (*right*).

TABLE 2

OUTCOME DATA OF PATIENTS WITH ISOLATED CLOSED HEAD INJURY*

	Whole Group (*n* = *109*)	With Pneumonia (*n* = *45*)	Without Pneumonia (*n* = *64*)	p Value†
Mortality (%)	20 (18)	6 (13)	14 (22)	0.26
Days ventilated	6.5 ± 4.9	8.2 ± 5.1	5.3 ± 4.3	0.001
Days intubated	15.9 ± 20.8	21.1 ± 24.6	12.2 ± 16.8	0.039
Days in ICU	8.6 ± 5.0	10.5 ± 5.4	7.2 ± 4.3	0.001
Days in hospital	27.6 ± 24.2	34.8 ± 27.6	22.5 ± 20.2	0.013

* Data expressed as mean ± SD.

† Probability of patients with pneumonia versus patients without pneumonia.

tively). Correspondingly, the length of intensive care unit (ICU) stay and the length of hospital stay were both significantly longer (10.5 ± 5.4 days to 7.2 ± 4.3 days, p = 0.001 and 34.8 ± 27.6 days to 22.5 ± 20.2 days, p = 0.01) (table 2).

Among the 45 patients who developed pneumonia, 36 developed it while being ventilated, 3 while still intubated but after MV, and 6 after extubation (table 3). No patient developed pneumonia after the seventh hospital day despite a mean hospital stay of nearly 4 wk. The proportion developing pneumonia while intubated and undergoing MV was minimally greater than the proportion developing pneumonia after extubation (p = 0.04).

When we divided the group by severity of cerebral injury using GCS ≤ 5T as a cutoff, we found that severe injury correlated with duration of MV, duration of tracheal intubation, and duration of ICU stay (table 4), but not with the development of pneumonia (figure 2).

Of the 34 initially comatose patients who were excluded because mechanical ventilation was required for less than 24 h, only one developed pneumonia. The GCS of this group on admission to the hospital was 5.9T ± 0.2.

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.

Although we used criteria for pneumonia similar to those in other studies, we recognize that the clinical syndrome may not represent bacterial pneumonia in all cases. The study of Fagon and colleagues (16) found that only one-third of the patients with the clinical syndrome 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 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 3

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

Hospital Day	1	2	3	4	5	6	7	8
On ventilator	4/109 (4%)	9/100 (9%)	15/76 (20%)	5/43 (12%)	1/30 (3%)	1/22 (5%)	1/17 (6%)	0/13 (0%)
Off ventilator Still intubated	—	—	0/3 (0%)	1/7 (14%)	0/8 (0%)	1/10 (10%)	1/11 (9%)	0/8 (0%)
Off ventilator Extubated	—	1/5 (20%)	0/14 (0%)	2/27 (7%)	0/30 (0%)	1/31 (3%)	2/29 (7%)	0/29 (0%)

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*

Severity		Days Ventilated		Days Intubated		Days in ICU
GCS on admission						
≥ 5T, n = 68	p = 0.001	7.6 ± 5.4	p = 0.004	19.9 ± 22.8	p = 0.004	9.5 ± 5.7
> 5T, n = 41		4.7 ± 3.1		9.2 ± 14.9		7.0 ± 3.3
GCS at 24 h†						
≤ 5T, n = 52	p = 0.001	7.7 ± 5.3	p = 0.002	22.0 ± 25.6	p = 0.008	9.5 ± 5.8
> 5T, n = 47		4.6 ± 3.3		9.2 ± 12.7		6.9 ± 3.5

Definition of abbreviation: GCS = Glasgow coma score.

* Data expressed as mean ± SD.

† GCS data not available on all patients at 24 h.

terial colonization and pulmonary infection (5, 9, 17). The mechanisms suggested by LaForce (22) with colonization of the lower respiratory tract with microorganisms (usually gram-negative rods), continuous microaspirations, and overcoming of lung defense mechanisms may lead to a later onset of pneumonia (19, 21) that mostly occurs after day 4.

The mean duration of MV in this study population (6.5 ± 4.9 days) was short compared with that in prior reports (6, 7, 18) involving patients with serious underlying conditions. Most of our patients were successfully weaned from the ventilator by day 10. One-third (36/109 patients) developed pneumonia while being ventilated — a high incidence in light of the short duration of MV. Given the fact that all pneumonia occurred within 1 wk of hospitalization, the daily incidence of ventilator-associated pneumonia was high during the first few days, especially on days 3 and 4 (20% and 12%, respectively). This phenomenon suggests that early aspiration at the time of injury or during emergency intubation may have led to the pneumonia.

The relative risk of developing pneumonia after discontinuation of MV but while still intubated was low (table 3). Three patients, all having been ventilated for 3 days and weaned but still intubated, developed pneumonia on the 4th, 6th, and 7th days of intubation, respectively. When adjusted for duration of illness, the relative risk of developing pneumonia while intubated and mechanically ventilated was greater than for intubation alone ($p = 0.04$). Thus, mechanical ventilation was not prophylactic and was associated with an increased risk of pneumonia. Of course we cannot rule out that continued mechanical ventilation was a marker for an associated problem, and, thus, cause and effect cannot be firmly established.

Overall, the mortality rate was low (18%) despite the high incidence of pneumonia. While most of the deaths (14/20 patients) occurred during the first week, this did not appear to be related to pneumonia. The young age of patients and the absence of underlying illness may be responsible for a favorable outcome after early-onset pneumonia (20). The lack of effect of pneumonia on mortality in isolated CHI differs markedly from the increase seen in the mortality of patients with underlying respiratory failure who develop pneumonia (23). However, the duration of MV, ICU stay, and hospital stay were all clearly increased by pneumonia (table 2).

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, H_2 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 H_2 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 patients 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.

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