Risk factors for nosocomial pneumonia in critically ill trauma patients

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Objective: To determine risk factors for nosocomial pneumonia in critically ill trauma patients.

Design: Prospective cohort study.

Setting: The trauma intensive care unit (ICU) of a 1500-bed tertiary-care hospital.

Patients: All critically ill trauma patients (n = 103) admitted consecutively between November 1995 and October 1996.

Interventions: A comparison of data recorded at the time of ICU admission and during the clinical evolution in patients with (n = 23) and without (n = 80) nosocomial pneumonia was made. Data referred mainly to possible risk factors were recorded; they also included factors related to pneumonia etiology and evolutive factors. Predictors of nosocomial pneumonia were assessed by logistic regression analysis.

Measurements and Main Results: The presence of significant growth on quantitative cultures of the protected specimen brush (≥10³ colony forming units/mL) was required to accept pneumonia as microbiologically proven, as well as the concurrence of a cohort of clinical and radiologic signs. Twenty-three (22.3%) patients developed nosocomial pneumonia. The mean age of these patients was 41.7 yrs; 18 of them (78.3%) were men. The microorganisms isolated in significant concentrations were *Acinetobacter baumanii* (ten cases), *Staphylococcus aureus* (11 cases), *Pseudomonas aeruginosa* (five cases), *Haemophilus influenzae* (two cases), and *Klebsiella pneumoniae*, *Citrobacter freundii*, *Serratia marcescens*, *Enterococcus* spp., *Enterobacter* spp., coagulase-negative *Staphylococcus*, and *Streptococcus intermedius* (one case each one). Risk factors for pneumonia by univariate analysis included nasogastric tube; continuous enteral feeding; prolonged mechanical ventilation (>1 day); use of H2-receptor antagonist, sucralfate, muscle relaxants, corticosteroids, barbiturates, and inotropic agents; positive end-expiratory pressure; intense sedation; re-intubation; tracheotomy; urgent brain computed tomography (CT) scan; craniotomy; iatrogenic event; and hyperventilation. The mortality rate was 43.5% (10 of 23) in the nosocomial pneumonia group and 18.8% in patients without nosocomial pneumonia (p = .02). Also, the mean stay in the ICU, the therapeutic charge (measured with total and mean punctuation of the Therapeutic Intervention Scoring System) and the complications, infectious and noninfectious, of the clinical evolution were significantly more frequent in patients with nosocomial pneumonia than in those without pneumonia (p < .05). In the multivariate analysis, continuous enteral feeding, craniotomy, prolonged mechanical ventilation (>24 hrs), use of positive end-expiratory pressure, and corticotherapy...
were independent predictors of nosocomial pneumonia.

**Conclusions:** It seems that factors related to the patient's clinical course, rather than variables registered on the first days of ICU admission, are those that would exert an influence on the development of nosocomial pneumonia in critically ill trauma patients. In this way, from our point of view, in our study the main risk factors are the use of prolonged mechanical ventilation (>4 hrs) and positive end-expiratory pressure. At the same time, we can conclude that the reduction of this infection incidence could decrease the mean stay in the ICU, the therapeutic charge, and the prognosis in terms of mortality and morbidity.

**Key Words:** intensive care unit; trauma; head injuries; facial injuries; femoral fractures; abdominal injuries; nosocomial pneumonia; protected specimen brush; mechanical ventilation; multivariate analysis

Hospital-acquired infections in patients admitted to the intensive care unit (ICU), particularly pneumonia, represent a major health problem because of the high incidence (between 20% and 40%) and the excess morbidity, mortality, and costs (1-7). It is well known that infections are the leading cause of late mortality in patients with severe trauma (8). A substantial reduction in morbidity, mortality, and costs could result from early identification of high-risk patients and institution of strategies to prevent the development of nosocomial infections (7, 9). Although risk factors for the development of nosocomial pneumonia (NP) in ICU patients have been assessed in multiple studies (10-19), results are frequently controversial mainly due to methodological differences. However, mechanical ventilation, histamine-2 (H2) receptor blocker use, prophylactic antimicrobial therapy, depressed consciousness, and massive gastric aspiration are the five variables usually identified as significantly associated with a higher risk for developing nosocomial pneumonia in ICU patients (6, 10-14). It is a paradox that, although a special importance is given to nosocomial pneumonia in polytrauma patients, there are few studies strictly related to this group of patients. Few investigations have specifically addressed the risk of nosocomial pneumonia development in targeted populations. For this reason, this prospective study was designed to assess risk factors for pneumonia in critically ill trauma patients.

**MATERIALS AND METHODS**

**Patients.**

The study population consisted of 103 patients consecutively admitted to the trauma ICU of a 1500-bed tertiary-care facility in Zaragoza, Spain, between November 1, 1995, and October 31, 1996. There were 78 men and 25 women with a mean age of 44.6 (SD 21.5) years.

All patients' main diagnosis was a serious trauma. They were, when admitted into the unit, in a critical situation, after urgent surgery or because they needed a close medical care for a variable time.

All patients were transferred from the emergency room directly to the trauma unit, although some patients were taken immediately to the operating room and were admitted after surgery. Lesions were categorized according to the main injury that was the reason for ICU admission. The head was involved in 51 cases, chest in 35, long bones of the extremities (except for the femur) in 33, pelvis/femur in 21, dorsolumbar vertebrae in 14, face in 13, cervical vertebrae in 12, and the abdomen in 11. Selective digestive decontamination was not used. The study was approved by the Institutional Review Board.
On the first day of ICU stay, the data compiled for each patient consisted of demographic data: preexisting conditions (obesity [0% excess over ideal weight], diabetes mellitus, current cigarette smoking [> 10 pack/yr], alcohol intake [>80 g of alcohol per day], drug abuse, severe chronic liver disease [having clinical and analysis alterations produced by this illness in its advanced phase], renal disease [glomerular filtration rate, ≤50 mL/min], chronic obstructive pulmonary disease [COPD] (20), and chronic immunosuppression), type of injury, occurrence of an iatrogenic event, and severity of illness using different scales, such as the Acute Physiology and Chronic Health Evaluation (APACHE) II (21), Simplified Acute Physiology Score system (SAPS) (22), Glasgow Coma Scale (23), and the trauma score (24). In all cases, the worst possible score obtained on this day was recorded.

The following variables were measured daily, before the onset of nosocomial pneumonia: nasogastric tube; continuous enteral feeding; drug therapy (H2-receptor antagonists, sucralfate, antacids, antibiotics, inotropic agents, corticosteroids, and immunosuppressive drugs); dialysis therapy; prolonged mechanical ventilation; use of positive end-expiratory pressure; orotracheal or nasotracheal intubation; re-intubation; difficulty of tracheal intubation (subjectively evaluated by the physician performing this procedure); tracheostomy; sedation, muscle relaxants, gastric aspiration, invasive monitoring (central venous pressure, pulmonary/pulmonary capillary wedge pressure, intracranial pressure, or cardiac output), and surgery (urgent/elective); ileus; gastrointestinal bleeding; and shock. In patients with head injury, the presence of intracranial hypertension was indirectly evaluated by the need for an urgent brain computed tomography (CT) scan, craniotomy, and the administration of mannitol or intravenous barbiturates. Patient outcome (dead/alive) was determined at trauma ICU discharge. Other factors recorded included the duration of ICU stay; total TISS (therapeutic intervention scoring system) score (TISS-t) (25); mean TISS (TISS-m) score per days of ICU stay; and the development of complications, such as renal, liver, heart, and/or respiratory failure, shock, coagulopathy, and nosocomial infection other than pneumonia.

In all cases under suspicion of nosocomial pneumonia, series of blood cultures were taken, as well as protected specimen brush (PSB) samples, as is always done in our ward. Before the sampling, any antibiotic treatment was stopped for 24 hrs.

**Definitions.**

A diagnosis of pneumonia was considered when roentgenographic evidence of new and persistent (>48 hrs) pulmonary infiltrates was detected, together with at least two of the following features: temperature higher than 38°C or hypothermia below 35°C, peripheral leukocytosis, (>5,000 per mm3 or a 25% increase in the circulating leukocytes from baseline), or leukocyte recount lower than 4000 per mm3; purulent respiratory secretions, and appearance or worsening of respiratory insufficiency (PaO2/FIO2 <200) (26). Moreover, the presence of significant growth on quantitative cultures of the bronchoscopic PSB (≥103 colony forming units (cfu)/mL) was required to accept the pneumonia as microbiologically proven (27). Pneumonia was considered nosocomial when its onset occurred 48 hrs after admission to the trauma ICU. The remaining patients who did not meet these criteria were considered as not having nosocomial pneumonia and were included in the control group. Chronic immunosuppression was defined as patients with any disorder associated with immunosuppression (human immunodeficiency virus infection, hematologic malignancy, etc.) or treated with high dose corticosteroids (≥15 mg/day of prednisone or equivalent) or immunosuppressant drugs. An iatrogenic event was an adverse event unequivocally and directly associated with a diagnostic or therapeutic maneuver before the patient's ICU admission. The presence of shock was determined by systolic blood pressure below 90 mm Hg,
requirement for vasopressor medications for >4 hrs, and urine output lower than 20 mL/hr during this period. A diagnosis of respiratory failure was made when the PaO₂ was <60 mm Hg with a FiO₂ ≥21%, as well as when the PaO₂/FiO₂ was <200 mm Hg in mechanically ventilated patients. Catheter-related infection was defined as growth >15 colonies on semiquantitative cultures of the tip of the catheter, urinary tract infection as urine culture with >10,000 cfu/mL, and surgical wound infection as local inflammatory signs together with bacterial growth in smears obtained from the wound.

Statistical Analysis.

The above-mentioned factors were evaluated in both groups: with and without nosocomial pneumonia. After that, these data were statistically treated.

The univariate analysis was done using the chi-square test ($\chi^2$) and the Fisher's exact test for qualitative variables and the Mann-Whitney $U$ test for quantitative variables as none of the quantitative variable follows a normal distribution (Kolmogorov-Smirnov test). The level of significance was set at $p < .05$. Variables were then subjected to multivariate analysis with a logistic regression procedure and forward stepwise selection of $p < .10$ after univariate testing in order to assess the independent effect of each variable on the development of nosocomial pneumonia. The maximum likelihood approach was used to estimate the weights of the logistic parameters.

We have rejected those confidence intervals that, in our opinion, were of no interest for this article, always thinking of the absolute regression coefficient.

RESULTS

Twenty-three (22.3%) of the 103 patients developed nosocomial pneumonia. The mean age of these patients was 41.7 yrs (SD 21.54); 18 (78.3%) were men and five were women. The microorganisms isolated in significant concentrations were Acinetobacter baumanii (ten cases), Staphylococcus aureus (11 cases), Pseudomonas aeruginosa (five cases), Haemophilus influenzae (two cases); Klebsiella pneumoniae, Citrobacter freundii, Serratia marcescens, Enterococcus spp., Enterobacter spp., coagulase-negative Staphylococcus, and Streptococcus intermedius (one case for each bacteria).

Risk factors for nosocomial pneumonia by univariate analysis are the nasogastric tube; continuous enteral feeding; mechanical ventilation (>24 hrs); use of H₂-receptor antagonist, sucralfate, muscle relaxants, corticosteroids, barbiturates, and inotropic agents; positive end-expiratory pressure; intense sedation; re-intubation; tracheotomy; urgent brain computed tomography scan; craniotomy; iatrogenic event; and hyperventilation (Table 1). Statistically, there were no significant differences between patients with nosocomial pneumonia and patients without nosocomial pneumonia in relation to demographic data, preexisting conditions, severity of illness, orotracheal intubation, need for intense respiratory physiotherapy, invasive monitoring, and dialysis therapy, previous antibiotic treatment, ileus, gastrointestinal bleeding, surgery, use of immunosuppressive drugs and administration of mannitol (Table 2).
On the other hand, the mean stay for the group control was 6.83 days (SD 6.65), whereas those with nosocomial pneumonia had a mean stay of 28.56 days (SD 26.06; p < .001; Mann-Whitney test). The overall mortality rate was 24.3% (25 of 103). The mortality rate was 43.5% (10 of 23) in the nosocomial pneumonia group and 18.8% (15 of 80) in patients without nosocomial pneumonia (p = .02) (Table 3).

Complications were also significantly more frequent in patients with nosocomial pneumonia than in those without pneumonia (shock 43.5% vs. 6.3%; renal failure 21.7% vs. 0%; heart failure 13% vs. 1.3%; hepatic insufficiency 8.7% vs. 0%; respiratory failure 91.3% vs. 10%; severe coagulopathy 26.1% vs. 2.5%; and infection other than pneumonia 60.9% vs. 5%) (p < .05).

In the multivariate analysis, continuous enteral feeding (odds ratio, 14.71, 95% confidence interval [CI], p = .0530); craniotomy (odds ratio, 218.81, 95% CI, p = .0055); prolonged mechanical ventilation (odds ratio 1.25, 95% CI, p = .0223); and use of positive end-expiratory pressure (odds ratio 36.74, 95% CI, p = .0072) were independent predictors of nosocomial pneumonia in ICU trauma patients. The use of corticosteroids showed an odds ratio of 14.91 (95% CI) with a p value of .0897.

**DISCUSSION**

The main problem with this type of study is how to identify the patients with pneumonia. It is well known the lack of sensibility and specificity of the radiologic and clinical parameters, but in daily practice it is impossible to find some other kind of identification (28, 29). Even the histological study,
considered as "reference technique," is not free from limitations (30). We use a definition for nosocomial pneumonia that combines the fulfillment of a series of clinical and microbiological criteria after taking the samples (PSB) because of its high specificity (28).

The important findings of this study are that 1) the incidence of nosocomial pneumonia (22.3%) is similar to that found in other studies that required quantitative culture of respiratory samples obtained by the protected telescoping catheter as a diagnostic criterion of respiratory tract infection (27); 2) despite the relatively low incidence of pneumonia, the mortality rate was remarkably high (43.5%), particularly in relation to high-risk causative microorganisms (P. aeruginosa, A. baumannii, S. aureus) (5); and 3) pneumonia prolonged ICU stay in trauma patients and was associated with a higher therapeutic intervention and greater frequency of complications. On the other hand, Baker et al. (31) identified trauma patients requiring prolonged hospitalization and incurring in higher costs but no excess mortality that could be attributed to pneumonia.

In this study, independent risk factors for nosocomial pneumonia in trauma patients were continuous enteral feeding, the need to perform a craniotomy, and the use of prolonged mechanical ventilation, especially with positive end-expiratory pressure. All these factors, together or individually, have been previously identified in other studies (9-13, 29). Prolonged mechanical ventilation with positive end-expiratory pressure was the most important risk factor in our study. The incidence of nosocomial pneumonia is 6 to 20 times greater in patients who receive mechanical ventilation via an orotracheal or nasotracheal tube (29, 31, 32). Fagon et al. (27) estimated that the incremental risk for developing pneumonia in mechanically ventilated patients is 1% per day of ventilation. Both orotracheal and nasotracheal tubes bypass natural host defenses, permit leakage of bacteria and secretions around the cuff into the trachea, damage the ciliated epithelium in the trachea, reduce bacterial clearance from the trachea, and, additionally, intubation maneuvers can ease the direct germs entrance into the airway tract (31, 32). But perhaps its true importance comes from the fact that, indirectly, it identifies the worse patients, precisely those suffering specific clinical situations (lung edema, low consciousness level) that may have a certain role in the onset of this infection (12). The relationship between the use of positive end-expiratory pressure and the development of pneumonia can be explained by the fact that positive end-expiratory pressure is mainly used to treat patients with acute respiratory distress syndrome or severe acute respiratory failure who are highly predisposed to nosocomial pneumonia (12). Similarly, the identification of craniotomy as a risk factor for nosocomial pneumonia may be related to the need for surgery in a subgroup of patients with especially severe closed-head injury, but at the same time, without an imminent fatal outcome due to the absence of concomitant injury or underlying medical illness (1).

As previously shown by others, continuous enteral feeding was a risk factor for nosocomial pneumonia. The administration of enteral feedings with high pH via the gastric tube may increase gastric colonization, volume, pressure, and reflux (33, 34). In relation to the importance of gastric pH in the gastric colonization by Gram-negative bacilli, treatment with H2 blockers did not increase the risk of pneumonia in our study. By contrast, Torres et al. (12) found a twofold increased risk of nosocomial pneumonia in patients treated with antacid and/or H2 blockers. Others (11, 15) have reported similar results. However, in a population of critically ill trauma patients, Simms et al. (35) did not find differences in either gastric bacterial colonization or the incidence of pneumonia in relation to treatment with antacids, H2 blockers, or sucralfate. On the other hand, other risk factors for developing nosocomial...
pneumonia, such as previous antibiotic therapy, severity of underlying disease, and age, which have been recognized in many studies, were not found statistically significant in our population.

It is not surprising for corticotherapy to be a risk factor, as, apart from its well-known anti-inflammatory and immunosuppressor effects, there are several studies associating its use with pulmonary infection development (1, 35).

In medical literature there is a wide fluctuation relating nosocomial pneumonias' incidence in these groups of patients, although it is generally very high (20% to 40%) (13, 15, 28, 34). This wide fluctuation is due to the variable influence of the different risk factors, patient characteristics, type of ICU where the study is developed, and, above all, the definition of pneumonia that is being used. In this way, incidence observed in our study is similar to the incidence reported in other studies, in which microbiological confirmation with PSB (28) was also used.

There is another aspect of our study to be considered: the patients with nosocomial pneumonia suffered a longer period of stay in ICU and had worse evolution, in morbidity and mortality. That brought about a higher mean therapeutic charge per day and, as a whole, during their stay in ICU (TISS-m and TISS-t). We consider that these conclusions have special implications in trauma patients. Perhaps for most of the critical patients this infection has no meaning in their prognosis, as their basic diagnosis is very serious (11); but in the cases that could be cured, the nosocomial pneumonia onset has a great impact on the rise of death rate (29). This idea is based on the experience of several cases where, although the use of selective intestinal decontamination may decrease the colonization and infection incidence, it only produces a decrease in the mortality rate of the trauma patients subgroup (36).

Although these conclusions were also emphasized by several authors, they have not been clearly demonstrated, as it is very difficult to distinguish how much mortality and health resources expenses are due to the gravity and type of base illness from that produced by the pneumonia itself (as a complication) (5, 11, 12, 29, 31, 37). Additionally, the "therapeutic effort" can act at the same time as a risk factor to develop an infectious complication. So, authors as Baker et al. reported in their study that pneumonia only produced a longer stay in hospital, but it did not produce higher mortality rate nor larger therapeutic effort (31).

It is necessary to comment that the mortality observed (43.5%), higher than the one registered in other series, arises, at least in part, from the fact that most of our pneumonias' origins were germs traditionally considered as "high-risk germs," such as *P. aeruginosa*, *A. baumannii*, and *S. aureus* (5, 27, 29).

In conclusion, whereas the factors from the first day of stay in the ICU do not have an influence on the development of pneumonia, the other factors derived from the illness evolution (prolonged mechanical ventilation, positive end-expiratory pressure, corticotherapy, craniotomy, and continuous enteral feeding) have a main role. If we could avoid these factors, perhaps in the future we could decrease the incidence of this illness as well as the mortality rate, the associated complications, and the amount of health resources invested.

As a final conclusion, we are aware of the dangers derived from these factors, and so, we think that by the intensification of the hygienic and prophylactic measures in the patients having some or several of these risk factors, we could reduce the incidence of this infectious complication and its mortality.
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