Journal of Hospital Infection 86 (2014) 53–56

Available online at www.sciencedirect.com

Journal of Hospital Infection

journal homepage: www.elsevierhealth.com/journals/jhin

Underlying illness severity and outcome of nosocomial pneumonia: prospective cohort study in intensive care unit

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ARTICLE INFO

Article history:
Received 11 June 2013
Accepted 23 September 2013
Available online 18 October 2013

Keywords:
APACHE II
Cohort study
Mortality
Nosocomial infection
Pneumonia

SUMMARY

Background: Previous studies have suggested that the final outcome of a patient with nosocomial pneumonia (NP) may depend on the patient's illness severity upon admission to the intensive care unit (ICU).

Aim: To investigate the relationship between developing NP during hospitalization in an adult ICU and the risk of death with special focus on illness severity at admission in the unit.

Methods: A prospective cohort study was performed among all patients admitted for at least 24 h to the ICU of a university reference hospital in Spain from 2006 to 2009. A stratified univariate study was performed according to the patients' illness severity at admission, estimated using the Acute Physiology And Chronic Health Evaluation (APACHE) II index. To determine whether the NP was independently associated with increased mortality in ICU, a multivariate logistic regression analysis was carried out, adjusting for potential confounders.

Results: In all, 4427 patients were studied, of whom 233 acquired NP while admitted. Patients who developed NP had a 2.6 higher risk (95% confidence interval: 2.1–3.0) of dying compared with those who did not develop NP. When stratified by the APACHE II index, the significant association remained at each stratum, although the strength of the association decreased as the value of the index increased. In the multivariate analysis, NP was independently associated with death in the ICU. The interaction between NP and the APACHE II index, with a negative coefficient, was also significant.

Conclusions: Developing NP while admitted to the ICU was independently associated with increased mortality. However, the strength of the association decreased as the severity of patient illness upon admission to the ICU increased, not influencing death of patients with severe APACHE II values.

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Introduction

Nosocomial pneumonia (NP) in adult intensive care units (ICUs) is a major public health problem that generates adverse

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http://dx.doi.org/10.1016/j.jhin.2013.09.014

consequences affecting patients' safety and quality of healthcare systems.[1–4] NP has become a priority in patient safety policies at the national and international levels, including international reference organizations, which are constantly in search of strategies for prevention and control of NP.[5,6]

One of the direct consequences of NP is the burden of disease it causes by overshadowing the initial diagnosis of the patient, increasing the potential risk of complications and death. It also causes personal suffering and temporary or permanent disability that can decrease the quality of life of patients in the future. The fact that NP increases the average stay of patients in the ICU, with increased costs for the healthcare system, has been well documented in previous investigations.[3] However, the relationship between NP and increased ICU mortality is controversial; whether NP is an added risk of mortality among patients in the ICU does not have a clear answer among clinicians and researchers.[7] The difficulty of assessing this association is partially due to the intrinsic characteristics of the infection. It mainly occurs in patients already in a critical condition, making it complicated to determine to which extent and with what intensity NP is responsible for a negative outcome. Previous studies suggest that the final outcome of a patient with NP may depend on the patient's illness severity upon admission to the ICU.[8,9] In order to provide new evidence, we investigated the relationship between developing NP during hospitalization in the ICU and risk of patient death in the unit with special focus on patients' severity at admission.

Methods

Study design and study population

We performed a prospective cohort study in the adult ICU at a university reference hospital in Spain, from January 2006 to December 2009. We included all patients admitted for at least 24 h. This tertiary referral hospital has 1301 beds and serves a population of about 1,450,000 inhabitants. The medical–surgical adult ICU has 34 beds, divided in six specialized modules, and has an average of 1300 admissions per year.

Data collection and variables

Using a prospective surveillance system, recognized as the one with the highest sensitivity and specificity for identification of nosocomial infections, the hospital's department of preventive medicine monitored all patients included in the study, from ICU admission up to 48 h after being discharged from the unit.[10,11] Upon admission, a data collection sheet that was filled in daily was completed for each patient. The sources of information used to complete the data collection sheet were clinical records, results of radiological examinations and laboratory tests, direct observation of the patients and healthcare staff consultations.

The following variables were collected for each patient: sex, age, death (up to 48 h after discharge from the ICU), NP (both ventilator-associated pneumonia and NP not related to ventilation) and nosocomial infection (other than NP). In order to diagnose nosocomial infections, and specifically NP, we used the criteria developed by the Centers for Disease Control and Prevention (CDC).[12]

The following confounding variables, which can be associated with both NP and death and are not part of the intermediary chain between NP and death, were collected.

- Intrinsic risk factors: patient characteristics present upon ICU admission: illness severity upon admission, measured by the Acute Physiology And Chronic Health Evaluation II (APACHE) II index, main diagnosis upon admission, defined according to the main categories of the International Classification of Diseases (9th revision); presence or absence of traumatic brain injury, coma, kidney failure, diabetes, antibiotic therapy prior to admission, malignancy, neutropenia, liver cirrhosis, malnutrition, infection prior to admission. Clinical criteria developed by the Spanish Prevalence Study of Nosocomial Infections (EPINE) were used to define these variables.[13,14]
- Extrinsic risk factors: diagnostic or therapeutic procedures performed while admitted: intake of H2 antagonists, proton-pump inhibitors or sedatives; immunosuppressive drugs; surgery; presence or absence of the following devices: bronchoscopy, gastroscopy, urinary catheter, peripheral line, central catheter, peripherally inserted central catheter, parenteral nutrition, tracheostomy, mechanical ventilation, biphasic positive airway pressure (BiPAP), continuous positive airway pressure, chest or surgical drainage, nasogastric tube, Swan–Ganz balloon, intra-aortic balloon pump.

Statistical analysis

The crude effect of NP on mortality was estimated with the relative risk (RR) obtained after performing a univariate analysis. A stratified univariate analysis recoded the APACHE II index into three different categories: low (<25th percentile), moderate (25th–75th percentiles) and severe (>75th percentile).

To determine whether the NP was independently associated with increased mortality in the ICU a multivariable logistic regression analysis was performed. The dependent variable in the model was death in the ICU (yes/no). Infection or not with NP and all those variables previously defined as potential confounders for potential inclusion were considered in the final model. All variables with $P \leq 0.25$ in the univariate analysis were included in the multivariate logistic regression model. We constructed the final multivariate model by performing backward stepwise manual selection. We conducted the Box–Tidwell test for continuous variables to identify possible interactions and potential confounders. All statistical analyses were performed using the Statistical Package for Social Science (SPSS) version 15.0 and STATA version 11.0 (Stata Corp., College Station, TX, USA).

Results

A total of 4427 patients was studied; 2923 (66%) were male and the mean age was 58.5 years (SD: 16.2). The median value of the APACHE II index was 16 (range: 2–47). The 25th and 75th percentiles were 13 and 20, respectively. A total of 233 patients developed NP (cumulative incidence: 5.3 per 100 admissions), of which 225 (96.6%) were ventilator-associated.

Of the patients that developed NP, 39.1% (91/233) died, compared with 15.3% (643/4194) among those that did not develop NP [RR: 2.6; 95% confidence interval (CI): 2.1–3.0].

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