Effects of isolation rooms on the prevalence of hospital acquired pneumonia in a respiratory ICU[#]

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Abstract. – BACKGROUND: The incidence of hospital acquired pneumonia (HAP) varies according to the type of intensive care units (ICUs).
   AIM: The aims of this study were to determine the frequency of hospital acquired pneumonia (HAP) and the effect of isolation rooms on the frequency of pneumonia in the ICU.
   MATERIALS AND METHODS: The present investigation was carried out between January 2004 and July 2008. The ICU, which was 4-bed ward-type between January 2004 and February 2006 (1st period), was reconfigured as isolated rooms with only 2 beds each after March 2006 (2nd period). 153 and 379 patients were followed up in the ICU in the 1st and 2nd periods, respectively. Blood, sputum, and deep tracheal aspiration cultures were used for the isolation of the causative agents.
   RESULTS: No significant difference was detected between the general characteristics of patients. HAP developed in 101 patients (19%). The prevalence of HAP was 22.9% in the 1st period and 17.4% in the 2nd period. During the 1st and 2nd periods, the HAP infection densities were 22.2 and 16.1/1000 patient-days and the ventilator-associated pneumonia densities were 48.1 and 37.6/1000 ventilator-days, respectively. Eighty-six percent of HAP was ventilator-associated pneumonia (VAP).
   CONCLUSIONS: Isolation rooms in the ICU may be an effective strategy to control and decrease the rate of pneumonia in the ICU in addition to other preventive strategies.

Key Words:
   Pneumonia, ICU, Isolation room, Clinical epidemiology, Infection control.

Introduction

Hospital-acquired pneumonia (HAP) are the most common nosocomial infections in intensive care units (ICUs). The risk for development of HAP is higher in the ICU than the other departments of the hospital[1]. While the overall prevalence of HAP is approximately 5-10 cases per 1000 admissions, the risk increases for patients in the ICU where the prevalence ranges from 9-37%[1-4]. The prevalence of HAP varies according to the differences in the definition of pneumonia, the type of the ICU, and to the characteristics of the patient. Ventilator-associated pneumonia (VAP) occurs in 9-27% of all intubated patients[1,3]. In ICU patients, nearly 90% of episodes of HAP occur during mechanical ventilation.

The crude mortality rate for HAP ranges from 25-50%[4,5]. Fifteen percent of all deaths that occur in hospitalized patients are directly related to nosocomial pneumonia. Due to the high mortality risk, legal issues, and ethical problems, it is important to determine the prevalence, as well as the causative agents and risk factors for HAPs, in an assessment of the actions to be taken.

Although, it is a general belief that the use of isolated rooms in the ICU decreases the frequency of HAP, few data are available to address the impact of ICU design on prevention of nosocomial infections. It has been reported that bronchopulmonary colonization by *Acinetobacter baumanii* is decreased in mechanically-ventilated patients in a surgical ICU and the prevalence of VAP is reduced in pediatric intensive care patients by being shifted to ICUs with isolated rooms[6,7].

In the present study, it was aimed to determine the prevalence, causative agents, antimicrobial resistance, and risk factors for lower respiratory tract infections in patients followed in the ICU for the last 4 years. The effect of reconfiguration from a ward-type ICU consisting one large room to an ICU with isolated rooms with two beds on the percentage of HAP was also determined.

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Materials and Methods

Settings

The present study was conducted between January 2004 and July 2008 in the respiratory ICU of a University Hospital. All of the patients (532 patients) who had been admitted to the ICU during this period were included in the study. Patients followed in ICU are; those with severe pneumonia, acute respiratory distress syndrome (ARDS) and severe chronic obstructive pulmonary disease (COPD). A physician is continuously on duty in the respiratory ICU and the nurse-to-patient ratio is one nurse per three patients. The study was approved by the Ethical Committee of the Hospital.

Definitions

The Centers for Disease Control (CDC) criteria were used for the diagnosis of pneumonia[8,9]. HAP was diagnosed by the presence of a new or progressive infiltration (different from the initial infection site) which occurred at least 48 hours after admission to the ICU, as well as the presence of at least two of the following: fever, leukocytosis, and an increase in tracheobronchial secretions[10]. Alternatively, the presence of significant growth ($>10^6$ cfu/mL: colony forming unit/mL) in the endotracheal aspirate (ETA) culture or growth of the same microorganism in blood cultures in addition to a new infiltration was also defined as HAP[11]. The microorganisms which were isolated as the causative agents were identified via standard microbiological methods.

The intubation criteria for the patients were defined prior to the study and invasive ventilation was performed in the presence of such criteria. Pneumonia that developed after the 48th hour of invasive ventilation was defined as VAP. For isolation of the causative agent in patients on invasive ventilation, an endotracheal aspirate (ETA) culture (mini-bronchoalveolar lavage: BAL) was performed within the first 24 hours using BAL-collecting containers. Sputum and blood cultures were performed for non-intubated patients.

The infection rates for HAP and VAP were calculated as the total number of episodes divided by the total number of patient-days ($\times$ 1000) and ventilator-days ($\times$ 1000), respectively. Only the first episode of pneumonia was included for the calculation of infection rates.

Proton pump inhibitors were used for gastric ulcer prophylaxis and low molecular weight heparin was used for pulmonary embolism prophylaxis in all patients. All of the patients who were considered to have HAP were given empirical antibiotic therapy according to the time of the pneumonia (early or late), as well as the presence of specific risk factors and the severity of the disease. Guideline recommendations have to be adapted to the local hospital flora and patterns of antibiotic sensitivity. The duration of antibiotic therapy was individualized depending on the severity of the illness and the rapidity of the clinical response.

Study Design

The ICU, which had a ward-type configuration with 4 beds (1st period, Figure 1a) from January 2004 until February 2006 was reconfigured as a unit with isolated rooms with 2 beds (6 beds total) in March 2006 (2nd period, Figure 1b). The general characteristics of the patients (age, gender, etc.), diagnosis at the time of hospitalization, physical examination and laboratory findings, concomitant diseases, and acute physiology and chronic health evaluation (APACHE) II scores, invasive procedures, type of nutrition, prophylaxis used, and the hospitalization periods were prospectively recorded on patient follow-up program of the ICU by the specialist.

Precautions

Strategies used to prevent the development of HAPs were as follows: using non-invasive mechanical ventilation, laying the patients at a 30º semi-recumbent position, use of peptic ulcer prophylaxis, washing hands before and after the examination of each patient, using ethanol-based hand disinfectants, and disposable surgical gloves and gowns. Those, in whom resistant infectious agents have been determined, were isolated in the rooms until the infection has been kept under control.

Statistical Analysis

The statistical analysis was performed with SPSS for Windows 12 (SPSS Inc., Chicago, IL, USA) statistical software. The significance level was considered as $p < 0.05$. During the first stage of the analysis, descriptive statistics were used to characterize the patient sample by mean and standard deviations (SD) of the eligible data. Quantitative variables were expressed by percentage. Variables were assessed for each patient using the c^2-test for categorical variables and an unpaired Student's t-test or Mann-Whitney U-test were used for continuous variables. A multivari-

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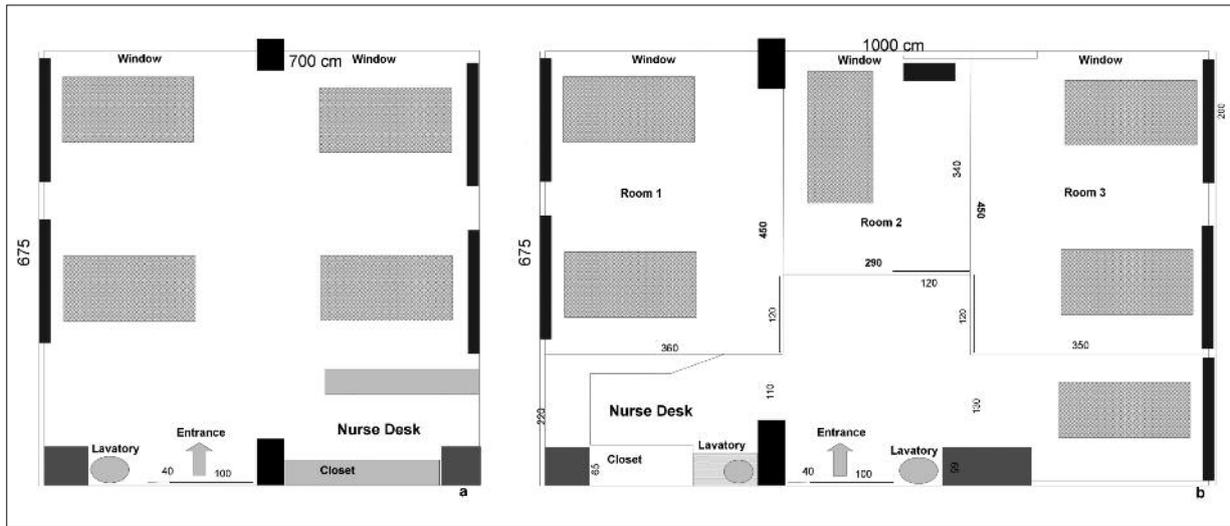
Figure 1. 1st and 2nd period schemas of the ICU.

ate logistic regression analysis model, along with backward stepwise analysis, was performed for patients with HAP to determine mortality-related factors. All comparisons of clinical and laboratory variables, with a *p*-value of < 0.05, were entered into the model by univariate analysis.

Results

The study cohort consisted of 532 patients (353 males and 179 females) with 5693 patient-days. The general characteristics of the patients and the indications for ICU admission are sum-marized in Table I. HAP developed in 101 of the patients (19.0%); 87 of them were VAPs. The prevalence of VAP was 28.6% in intubated patients. Of the 101 episodes of HAPs, 97% were classified as late onset. The prevalence of HAP was 17.7 cases per 1000 patient-days and the prevalence of VAP was 40.9 cases per 1000 ventilator-days. The crude mortality rate for patients with HAP was 66.3% (67 of 101).

The median period from intubation to VAP diagnosis was 6 days (range, 4-15 days). The length of ICU stay was significantly longer in patients with HAP (8.8 days vs. 23.6 days; *p* < 0.001). No significant difference was observed

Table I. Distribution of general characteristics of the patients and the indications for ICU admission.

	Overall patients (n = 532)	HAP		*p*
		Present (n = 101)	Absent (n = 431)	
M/F	353/179	64/37	289/142	NS
Age, years (mean ± SD)	64.1 ± 14.1	64.3 ± 14.3	64.1 ± 14.1	NS
Indications for ICU admission (%)				NS
COPD acute attack	305 (57.3%)	59 (58.4%)	246 (57.1%)	
Pneumonia	138 (25.9%)	32 (31.7%)	106 (24.6%)	
CHF	58 (10.9%)	5 (5.0%)	53 (12.3%)	
Others	31 (5.8%)	5 (5.0%)	26 (6.0%)	
Duration of ICU stay, days (mean ± SD)	10.7 ± 9.4	23.4 ± 13.2	8.2 ± 5.6	< 0.001
Applied IMV, n (%)	304 (57.1)	87 (86.1)	217 (50.3)	< 0.001
APACHE II score (mean ± SD)	22.3 ± 5.3	26.7 ± 6.1	21.3 ± 4.5	< 0.001

HAP: Hospital-acquired pneumonia; M/F: male/female; ICU: Intensive care unit; IMV: Invasive mechanical ventilation; APACHE II: Acute physiology and chronic health evaluation score II; NS: Not significant.

between the patients with and without HAP in terms of age, gender, and indications for ICU admission (Table I).

Culture samples were obtained from 96 of 101 patients diagnosed with HAP, and the agents for pneumonia were isolated in 81 patients (80.2% of HAPs). The most frequently isolated agents were *Acinetobacter baumanii* and methicillin resistant *Staphylococcus aureus* (MRSA). While the resistance to methicillin was 53% for *Staphylococcus aureus* (MRSA), the resistance against vancomycin was not determined.

One hundred fifty-three patients were followed in the ICU during the 1st period, whereas 379 patients were followed in the 2nd period. No differences existed between the patients in terms of age, gender and severity scores. The hospital mortality rate was 33.3% in the 1st period and 33.5% in the 2nd period (Table II).

During the 1st period, the prevalence of HAP in the ward-type ICU was 22.9%, whereas during the 2nd period the prevalence of HAP was 17.4% (absolute risk reduction, 5.5%; relative risk reduction, 24%) ($p = 0.18$). The prevalences of HAP were 22.2 and 16.1 cases per 1000 patient-days for the 1st and 2nd periods, respectively, and the prevalences of VAP were 48.1 and 37.6 cases per 1000 ventilator-days for the 1st and 2nd periods, respectively (Figure 2).

Based on multivariate analysis, the most significant risk factors for developing HAP were invasive ventilation (OR, 3.26; CI, 1.40-7.57) and long-term ICU stay (OR, 1.24; CI, 1.18-1.31). Apart from this, it was observed that the effect of aspiration and high APACHE II score were not independent from other factors.

Discussion

Despite the hypothesis that isolated rooms in the ICU would decrease the prevalence of HAPs, few data are available to address the impact of ICU design on the prevention of nosocomial infections.

The percentage of infections ranges from 9-37% according to the type of the ICU, as well as the patient profile[4,12]. In the present study, the prevalence of pneumonia was 22.9% during the 1st period, whereas the prevalence of pneumonia decreases to 17.4% during the 2nd period of the study ($p = 0.18$). Mulin et al[6] demonstrated a lower rate of bronchopulmonary colonization with *A. baumanii* among mechanically-ventilated patients in a surgical ICU after the unit was configured from one with a mixture of enclosed isolation rooms and open rooms to all enclosed rooms with handwashing facilities. Another study[7] demonstrated a reduction in the incidence of VAP in a pediatric ICU after it was converted from an open ward to separate isolation rooms, without a significant change in patient-to-staff ratios.

In a multicenter study[13], the prevalence of VAP was 18.9% and the infection density was found

Table II. Distribution of general characteristics of the patients in 1st and 2nd periods.

	1st period (n = 153)	2nd period (n = 379)	p
M/F	108/45	245/134	0.22
Age, year (mean ± SD)	62.3 ± 14.6	64.9 ± 13.8	0.06
Indications for ICU admission			NS
COPD Acute Attack	93 (60.8%)	212 (55.9%)	
Pneumonia	23 (15.0%)	115 (30.3%)	
CHF	20 (13.1%)	38 (10.0%)	
Others	17 (11.1%)	14 (3.7%)	
Duration of ICU stay, day (mean ± SD)	10.3 ± 8.5	10.9 ± 9.4	0.24
Applied IMV n (%)	95 (62.1)	209 (55.1)	0.15
APACHE II score (mean ± SD)	22.1 ± 4.9	22.4 ± 5.1	0.75
HAP prevalence n (%)	35 (22.9)	66 (17.4)	0.18
Hospital mortality n (%)	51 (33.3)	127 (33.5)	0.99
HAP mortality n (%)	24 (68.6)	43 (65.2)	0.83

M/F: Male/female; ICU: Intensive care unit; HAP: Hospital-acquired pneumonia; COPD: Chronic obstructive pulmonary disease; CHF: Congestive heart failure; IMV: Invasive mechanical ventilation; APACHE II: Acute physiology and chronic health evaluation score II.
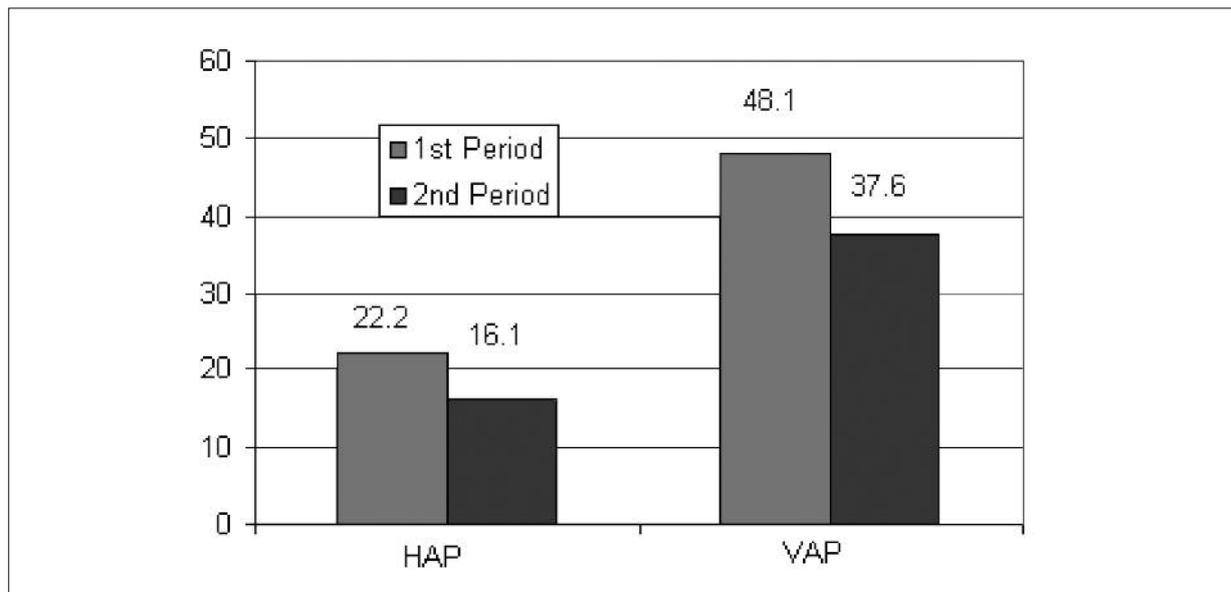
Figure 2. Infection densities of HAP (hospital-acquired pneumonia) and VAP (ventilator-associated pneumonia) in 1st and 2nd periods (densities in 1000 patient-days and in 1000 ventilator-days).

to be 26.5/1000 ventilator days. In the present study, the prevalence of HAP was 17.7 cases per 1000 patient-days, and the prevalence of VAP was 40.9 cases per 1000 ventilator-days. Of the pneumonias, 86.1% were found to be associated with invasive ventilation. Similarly, in a multi-center study performed by Suka et al[14]) in 2007, including 28 ICUs, it was reported that 87.4% of the HAPs were associated with ventilation and the overall HAP and VAP rates were reported as 6.5 and 12.6 cases per 1000 days, respectively. Previous multicenter cohort studies had reported the following lower infection rates for VAP: 14.8 cases per 1000 ventilator-days in Canadian ICUs[14], 13.3 cases per 1000 ventilator-days in 89 German ICUs[16], and 9.4 cases per 1000 ventilator-days in French ICUs[17].

It is difficult to precisely diagnose HAP or VAP due to the lack of a gold standard. The CDC criteria or modified criteria are used in many publications. The HAP criteria used in the present study were a new or a progressive infiltration occurring at least 48 hours after hospitalization in the ICU and the presence of at least 2 clinical signs[8,9]. Radiographic criteria alone have a 32% incidence of misdiagnosis. As a result of these difficulties, a diagnostic scoring system, the clinical pulmonary infection scores (CPIS), was developed[18,19]. Overall, the specificity of the CPIS is moderate and needs to be complemented by microbiological information for the manage-

ment of patients. In the present study as well, the diagnosis of pneumonia was verified by microbiological data.

In ventilated patients, the recommended approach is to obtain an ETA sample, or bronchoscopic or blind samples for quantitative cultures when there is a clinical suspicion of HAP[1,20]. Although the sensitivity of ETA is generally considered high, the specificity has been limited in part by contamination with upper airway bacteria in up to one-fourth of specimens. Quantitative cultures $> 10^6$ cfu/mL correlate with the presence of pneumonia[4,10,21].

Most episodes of pneumonia are attributed to aspiration of oropharyngeal secretions into the distal airways[22]. The best known methods used in reducing the rate of ICU infections are hand washing or using hand disinfectant solutions, educating the staff, avoiding unnecessary antibiotic use and maintaining head elevation by semi-recumbent positioning of the patient[23,24]. Despite all these precautions, ongoing infections give rise to the thought of some other influencing factors. As in the present study, configuration to an ICU with two beds or isolated rooms can provide a decrease in the incidence of infection.

In the present study, the mortality rate in patients with HAP was 66.3%, whereas the mortality rate was 25.8% in patients without HAP ($p < 0.001$). Bercault et al[25] reported the mortality rates in patients with and without ICU-acquired

pneumonia as 41% and 14%, respectively. Similarly, Heyland et al[26] also reported the mortality in patients with and without ICU-acquired pneumonia as 23.7% and 17.9%, respectively. However, in a multicenter study with large number of patients[27], no difference was reported between the patients with and without VAP in terms of mortality rates (38.1% and 37.9%, respectively).

Initiating appropriate broad-spectrum antibiotic therapy to the patients diagnosed with HAPs in the early stage positively affects the survey[1,28-29]. In our Clinic, sputum and blood cultures were collected from the patients considered to have HAPs, as well as ETA cultures from those intubated, within the first 24 hours[1,21,30].

Enteric Gram-negative bacilli and *Staphylococcus aureus* are reported to be the most common microorganisms causing HAPs[4,31]. In patients who required prolonged mechanical ventilation, enteric Gram-negative bacilli and MRSA are the most common etiological agents[32]. In our Clinic, the most frequently isolated microorganisms in HAP patients were *Acinetobacter* and MRSA. Prolonged hospitalization, exposure to broad-spectrum antibiotics, and multi-bed ICUs with no barriers between patients increase the risk of infection with MRSA. Leblebicioglu et al[13] reported that the most frequently isolated agents of VAP were *Acinetobacter* spp. (29.2%), *Pseudomonas* spp. (26.7%), *and Staphylococcus aureus* (24.2%).

The antibiotic resistance rates of HAP agents, which have been isolated in our clinic, were quite high. For example, in HAP patients, from whom *Acinetobacter* was isolated, resistance to fluoroquinolone and imipenem were 74% and 53%, respectively, whereas resistance to methicillin was 53% in patients from whom *Staphylococcus aureus* was isolated. Although in the present study high methicillin resistance was consistent with the results of the studies performed in countries such as Japan, methicillin resistance was higher than the reported averages of 5-40% in the US[33,34].

The frequency and role of fungi are not well known. However, in one postmortem study, the prevalence of *Candida* spp. was found 8%[1]). In the present study as well, the prevalence of *Candida* infection was 8.9%. In the study conducted by Leblebicioglu et al[13], the prevalence of *Candida* spp.-related VAP has been reported to be 2%.

Currently, the well-accepted measures of prophylaxis include hand-washing, adequate disinfection of respiratory equipment. In addition to these precautions, certain arrangements, such as configuration to an ICU with isolated rooms that would contribute to improve hand-washing habits of the staff, may have a significant impact on infection control.

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