Original Article

Impact of the implementation of a therapeutic guideline on the treatment of nosocomial pneumonia acquired in the intensive care unit of a university hospital*

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Abstract

Objective: To evaluate the impact that the implementation of therapeutic guidelines has on the empirical treatment of nosocomial pneumonia. **Methods:** A clinical trial, using historical controls and involving current ICU patients who had acquired nosocomial pneumonia, was carried out from June of 2002 to June of 2003. All were treated according to therapeutic guidelines developed by the Commission for Nosocomial Infection Control of the institution (group with intervention). As controls, the medical charts of the patients who acquired nosocomial pneumonia between June of 2000 and June of 2001 (group without intervention) were analyzed. Mortality and mean treatment period, as well as the length of hospital and ICU stays, were determined for the patients who acquired nosocomial pneumonia. **Results:** Mortality associated with pneumonia was lower in the group treated according to the therapeutic guidelines (26 *vs.* 53.6%; p = 0.00). As for overall mortality, there was no statistically significant difference between the two periods (51 *vs.* 57.9%; p = 0.37). There was also no difference in the type of microorganisms isolated, treatment period, length of hospital stay or length of ICU stay. **Conclusion:** The implementation of therapeutic guidelines for the treatment of nosocomial pneumonia acquired in the ICU can be efficacious in decreasing mortality rates.

Keywords: Pneumonia/treatment; Cross infection; Intensive care units; Mortality.

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Introduction

Nosocomial pneumonia is defined as a lower respiratory tract infection that affects the lung parenchyma and occurs 48 h or more after admission to the intensive care unit (ICU).[1] Although there have been technological advances in ventilatory support and the identification of new pathogens, as well as in the development of new antimicrobial agents and vaccines, ICU-acquired pneumonia remains common and severe.[1,2] More than half of all antibiotics prescribed in the ICU are for such pneumonia.[3]

The early initiation of appropriate empirical treatment is essential to optimizing patient recovery and reducing mortality.[1,4] Recent studies suggest that the prevalence of multidrug-resistant bacteria is high among patients with ICU-acquired pneumonia, implying a worse prognosis.[5,6] Prescription of antimicrobial agents should follow priorities such as severity of the disease, drug efficacy, previous use of antibiotics, presence of comorbidities, resistance patterns of in-hospital microorganisms, duration of hospital stay, epidemiological impact, and costs.[7]

Therefore, in order to guide physicians in the treatment of patients with ICU-acquired pneumonia and avoid the excessive use of antibiotics, with the consequent increase in resistant microorganisms responsible for more severe infections,[8] it is important to adopt therapeutic guidelines. These therapeutic guidelines should be based on the current situation (population and institution), evidence-based data, and the experience of health professionals specializing in the area.[9]

Despite the relevance of their use and the fact that they are widely studied in the literature, therapeutic guidelines have yet to gain acceptance, because physicians are afraid of losing their autonomy, as well as because there are no conclusive data regarding their efficacy.[8]

The principal objective of this study was to evaluate the impact of the use of therapeutic guidelines on overall infection-related mortality in patients with ICU-acquired pneumonia. Other objectives were to evaluate the duration of hospital stays and of treatment.

Methods

A clinical trial, with a historical control group, was carried out in the adult ICU of a university hospital. based on consensus from the American Thoracic Society[10] and the Brazilian Thoracic Society[11], as well as on frequency and sensitivity data for isolated microorganisms, The *Comissão de Controle de Infecção Hospitalar* (CCIH, Cross Infection Control Committee) of the State University at Londrina University Hospital, developed therapeutic guidelines for the treatment of pneumonia (Figure 1a, 1b). Severe pneumonia was defined using the American Thoracic Society[1] criteria, which include two or more of the following: admission to ICU; fraction of inspired oxygen higher than 35% or requiring mechanical ventilation (MV); progressive infiltration detected in X-rays; multilobar pneumonia or presence of cavitations; evidence of severe sepsis with hypotension or organ dysfunction; use of vasopressor agents for more than 4 h; decrease in urine production to < 20 mL/h or requiring dialysis. When none of these criteria were met, the pneumonia was considered mild. When only one was met, the pneumonia was considered moderate. The following clinical criteria were used to define worsening of the condition or a lack of improvement: fever; leukocytosis; purulent secretion; changes in the radiological and oxygenation profiles; and unresolved organ dysfunction.[1] The treatment period recommended in the therapeutic guidelines is 14 days. The intravenous antibiotic doses, as well as their adjustments for creatinine clearance (CrCl) below 10 mL/min, from 10 to 50 mL/min, and above 50 mL/min, are described as follows: amikacin 15 mg/kg/day (CrCl < 10: 20-30%; CrCl 10-50: 30-70%; CrCl > 50: 70-100%); cefepime 1-2 g 12-12 h or 8-8 h (CrCl < 10: 1 g 24-24 h; CrCl 10-50: 2 g 12-12 h or 24-24 h; CrCl > 50: 2 g 8-8 h or 12-12 h); ciprofloxacin 200-400 mg 12-12 h or 8-8 h (CrCl < 10: 50%; CrCl 10-50: 50-75%; CrCl > 50: 100%); clindamycin 600 mg 6-6 h or 900 mg 8-8 h (CrCl < 10: 100%; CrCl 10-50: 100%; CrCl > 50: 100%); imipenem 0.5-1 g 8-8 h or 6-6 h (CrCl < 10: 0.125-0.25 g 12-12 h; CrCl 10-50: 0.25 g 6-6 h or 12-12 h; CrCl > 50: 0.25-0.5 g 8-8 h or 6-6 h); levofloxacin 500 mg/d (CrCl < 10: single 500-mg dose followed by 250 mg 48-48 h; CrCl 10-50: single 500-mg dose followed by 250 mg 24-24 h or 48-48 h; CrCl > 50: 100%); meropenem 1-2 g 8-8 h (CrCl < 10: 0.5 g 24-24 h; CrCl 10-50: 1 g 12-12 h; CrCl > 50: 100%); metronidazole 500 mg 8-8 h (CrCl < 10: 50%; CrCl 10-50: 100%; CrCl > 50: 100%); piperacillin/tazobactam

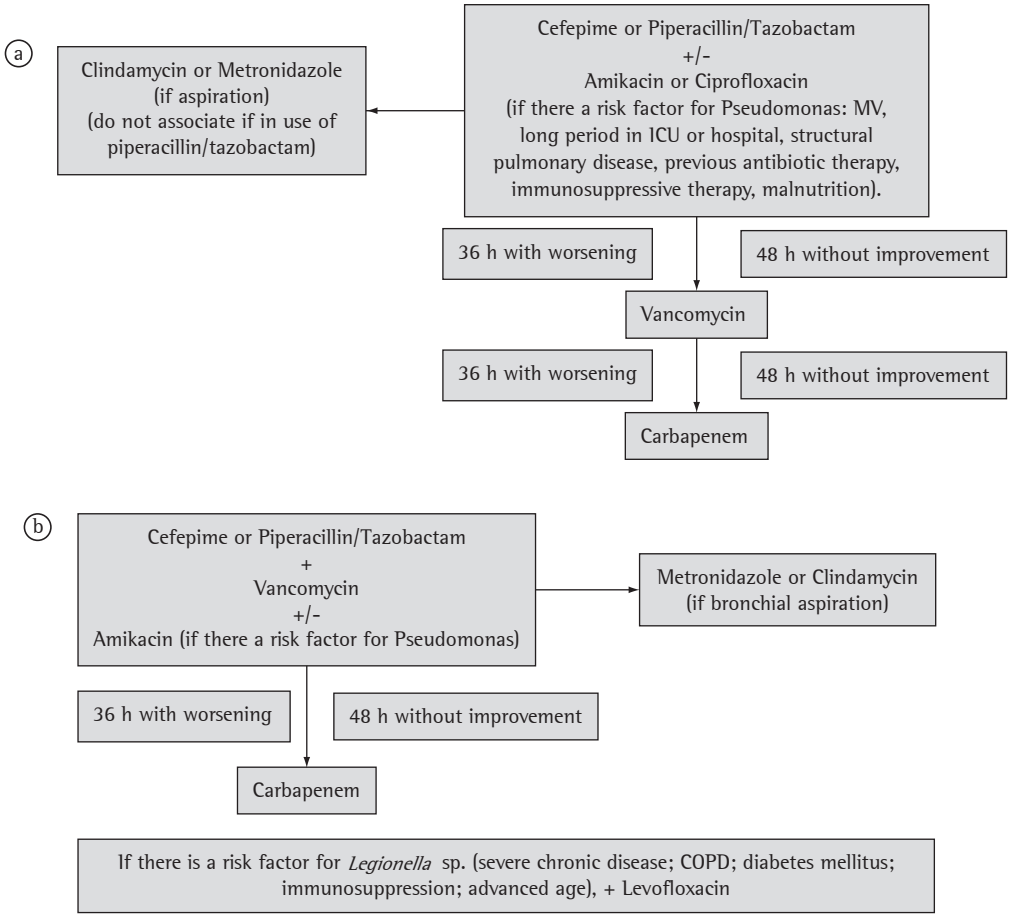

Figure 1 - a) Therapeutic guidelines for stable patients with mild to moderate pneumonia, without mechanical ventilation; and b) unstable patients with severe pneumonia. ICU: intensive care unit; COPD: chronic obstructive pulmonary disease.

4.5 g 8-8 h or 6-6 h (CrCl < 10: 2.25 g 8-8 h; CrCl 10-50: 2.25 g 6-6 h; CrCl > 50: 100%).

All patients older than 14 years of age and diagnosed with nosocomial pneumonia were included in the study. The diagnosis was based on chest X-rays with new pulmonary infiltrate or evolution of existing infiltrate and two or more of the following criteria established by the Centers for Disease Control[12]: leukocytosis (>12,000/mm^3) or leukopenia (<4,000/mm^3); fever (>38 °C) or hypothermia (<35 °C); and purulent tracheal secretions. Neutropenic patients (leukocytes < 1000 cells/mm^3 or neutrophils < 500 cells/mm^3) were excluded, as were transplant patients using immunosuppressants, patients under corticosteroid treatment for more than one month, patients who developed nosocomial pneumonia at other facilities, and patients transferred to other hospitals.

All patients who acquired pneumonia in this ICU between June of 2002 and June of 2003 (intervention period) were included in the study. They were monitored until discharge or death. The diagnosis of pneumonia and the application of the therapeutic guidelines in these patients were conducted by the attending intensivist responsible for the case, under from the guidance of the CCIH physician.

Data regarding historical controls (patients acquiring pneumonia during the nonintervention period) were collected through retrospective analysis of the medical charts of all patients admitted to the ICU between June of 2000 and June of 2001. Those of patients having developed nosocomial pneumonia in the ICU, as diagnosed by the attending intensivist, were selected. The retrospective definition of pneumonia followed the same

Centers for Disease Control criteria,[12] which were investigated in the medical charts and in the CCIH registration forms. This period was chosen because it provided a sample with characteristics similar to those of the intervention group, since during June of 2001 and June of 2002 administrative problems occurred, with changes in the proportion between the number of employees in the health professionals team and the number of patients, thus creating a confounding variable.

Data collected at inclusion were as follows: identification data - admission dates (hospital and ICU), date of pneumonia diagnosis, reason for admission to hospital, and reason for admission to ICU; presence of comorbidities; previous antibiotic therapy (type and duration of use); clinical data - arterial blood pressure, pulse, temperature, heart rate, and respiratory rate; acute physiology and chronic health evaluation II score (APACHE II); previous MV; nasogastric tube; use of drugs that alter gastric pH; previous surgery; laboratory data - blood workup, arterial blood gas analysis, sodium, potassium, creatinine, blood culture (two samples), bronchoalveolar lavage, quantitative culture for tracheal secretion. The bronchoalveolar lavage fluid was collected using fiberoptic bronchoscopy and was considered positive at $\geq 10^4$ cfu/mL, and quantitative tracheal aspirate was considered positive at $\geq 10^6$ cfu/mL.

In the clinical evolution of the intervention group, we evaluated the following: fever; quantity and aspect of the tracheal secretion (subjective assessment of the multiprofessional team); general health status; antimicrobial agents (type and period of use); MV and its duration; surgery; chest X-rays every 3 days or at shorter intervals when necessary; and outcome, defined as discharge (from the ICU and from the hospital) or death. In the nonintervention group, these variables were investigated in medical charts and the specific CCIH forms. In this group, the treatment evaluation and the decisions regarding changes in the antibiotic treatment regimen were carried out by the attending intensivist together with the physician responsible for the CCIH. This was the routine of prescription at the time.

Pneumonia-related mortality was defined as death in which nosocomial pneumonia was listed as the direct cause, and death unrelated to pneumonia was defined as death from other causes. Maintaining records for pneumonia-related deaths and deaths unrelated to pneumonia are part of the CCIH routine. A cross-check was performed with death certificate data.

The collected data was transferred to the Epi Info program, version 3.2 (Feb/2004), in order to perform the descriptive and analytical statistical analysis. In order to compare the numeric variables, the Student's t-test (normal distribution data) and the Mann-Whitney test (non-normal distribution data) were used. To compare the categorical variables, the chi-square test and the Fisher's exact test were used. The Mantel-Haenszel test was used for the stratified analysis. The adopted significance level was 5% ($p < 0.05$), and a 95% confidence interval was adopted.

This study was approved by the Ethics in Research Committee of the State University at Londrina University Hospital according to resolution CNS 196/96 (process CEP 069/02).

Results

In the nonintervention period, 81 patients were analyzed, 12 of which were excluded from the study. In the intervention period, 102 patients were analyzed, 6 of which were excluded from the study, according to the exclusion criteria (Figure 2), resulting in a sample of 165 patients analyzed.

Table 1 shows that the demographic and clinical characteristics were similar in both groups. In both periods, the most common diagnosis at admission was skull-brain trauma and cerebral vascular accident, with no difference between both groups. The studied population presented similar severity of the disease, observed by APACHE II. The most frequent comorbidities were diabetes, chronic obstructive pulmonary disease, heart failure, and kidney failure.

There was no difference between the two periods in terms of the date of pneumonia onset, clinical signs in diagnosis, and time on MV. The most common clinical signs in the intervention group were as follows: tachycardia (in 84.4%); tachypnea (in 66.7%); purulent expectoration (in 60.4%); and hyperthermia (in 47.9%).

Most pneumonia cases had an early onset. Of the 165 patients, 122 (73.9%) were placed on MV before the pulmonary infection. The use of MV before pneumonia was higher in the intervention group (83.3%; $p = 0.05$). Regarding other risk

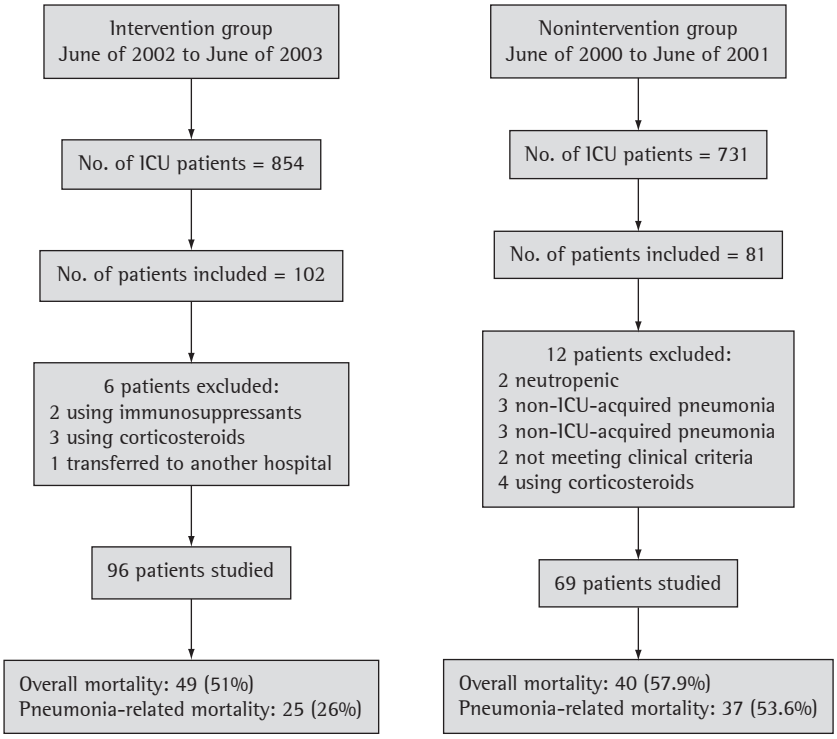

Figure 2 - Diagram of patients included in this study and description of mortality rates. ICU: intensive care unit.

factors, there was no difference between the two groups, except for the H+ proton pump inhibitors, which were more often used in the intervention period (p = 0.01) (Table 1).

Most patients in the intervention group (56.3%) received antibiotic therapy before the onset of pneumonia, and 53.7% received antibiotic therapy during the 5 days before the onset of pneumonia. After the implementation of the therapeutic guidelines, there was a significant decrease in the administration of cefepime, clindamycin, amikacin, and ceftriaxone (p = 0.00), as well as an increase in the administration of vancomycin (p = 0.02), piperacillin/tazobactam (p = 0.00), and chloramphenicol (p = 0.02). In 9 of the intervention group patients, the first antibiotic administered was carbapenem, since these patients developed pneumonia while under treatment with cefepime or piperacillin/tazobactam for infection at another site. The mean treatment period was similar in both groups: 16.6 ± 12.2 days (intervention group); and 17.6 ± 15.8 days (nonintervention group) (Table 2).

In the culture of tracheal aspirate, 39% of the nonintervention group patients tested positive, compared with 47.9% of the intervention group patients. Similar microorganisms were found in both groups: methicillin-resistant *Staphylococcus aureus*, *Pseudomonas aeruginosa*, *Acinetobacter* sp., and *Stenotrophomonas maltophilia*. Bronchoalveolar lavage fluid was collected from 13 patients, all in the intervention group. There was no significant difference between the groups regarding the stay in the ICU and hospital. The mean ICU stays were 18.7 ± 17.2 days (nonintervention period) and 16.0 ± 12.2 days (intervention period). The mean hospital stays were 32 ± 29.9 days (nonintervention period) and 26.3 ± 17.3 days (intervention period) (Table 3).

Pneumonia-related mortality was lower in the group treated according to the therapeutic guidelines (p = 0.00). Of the 69 historical control patients, 40 (57.9%) died, the principal cause of death being listed as pneumonia for 37 (53.6%). In the nonintervention period, 29 (42.1%) of the patients were discharged from hospital. In the intervention period, 49 (51%) of the 96 patients died, the principal cause of death being listed as pneumonia for 25 (26%).

Table 1 - Clinical characteristics of patients with ICU-acquired pneumonia at the State University at Londrina University Hospital according to the implementation of therapeutic guidelines. Londrina, Brazil, 2004.

Characteristic	Nonintervention (n = 69)	Intervention (n = 96)	p value
Age (years)	53.6 ± 19.6	52.0 ± 21.6	0.70
Stratified age			
Up to 50 years	29 (42.0%)	43 (44.8%)	0.84
>50	40 (58.0%)	53 (55.2%)	
Gender			
Male	42 (60.9%)	61 (63.5%)	0.85
Female	27 (39.1%)	35 (36.5%)	
Cause of admission to ICU			
SBT	15 (21.7%)	30 (31.2%)	0.66
CVA	10 (14.5%)	13 (13.5%)	-
Postoperative recovery	20 (29.0%)	22 (22.9%)	0.48
Hemodynamic instability	12 (17.4%)	10 (10.4%)	0.28
Respiratory failure	12 (17.4%)	2 (2.1%)	0.00
CHF	10 (14.5%)	8 (8.3%)	0.31
Comorbidity			
No	32 (46.4%)	32 (33.3%)	0.12
Yes	37 (53.6%)	64 (66.7%)	
Type of comorbidity			
Diabetes	11 (15.9%)	16 (16.7%)	0.93
COPD	10 (14.5%)	10 (10.4%)	0.58
Heart failure	10 (14.5%)	15 (15.6%)	0.98
Kidney failure	10 (14.5%)	9 (9.4%)	0.46
CVA	6 (8.7%)	18 (18.8%)	0.11
Other	23 (33.3%)	44 (45.8%)	0.14
Surgical intervention			
Elective	16 (23.5%)	18 (18.8%)	0.58
Emergency before pneumonia	14 (20.6%)	34 (35.8%)	0.05
Emergency after pneumonia	10 (14.7%)	7 (7.3%)	0.20
APACHE II	30.0 ± 6.9	29.2 ± 8.8	0.22
Time before diagnosis (days)			
Early (≤4)	51 (73.9%)	71 (74.0%)	0.86
Late (>4)	18 (26.1%)	25 (26.0%)	
Clinical signs at diagnosis			
Tachycardia	56 (81.2%)	81 (84.4%)	0.74
Purulent expectoration	41 (59.4%)	58 (60.4%)	0.97
Tachypnea	38 (55.1%)	64 (66.7%)	0.18
Hyperthermia	29 (42.0%)	46 (47.9%)	0.55
Hypotension	20 (29.0%)	23 (24.0%)	0.58
Hypothermia	7 (10.1%)	5 (5.2%)	0.37
Extrapulmonary infection	3 (4.3%)	13 (13.5%)	0.09
Bronchial aspiration	2 (2.9%)	4 (4.2%)	0.99
Mechanical Ventilation			
Before pneumonia	48 (69.6%)	80 (83.3%)	0.05
After pneumonia	10 (14.5%)	7 (7.3%)	0.21
Time on mechanical ventilation (days)	10.1 ± 9.9	11.0 ± 9.1	0.47
Other risk factors			
Nasogastric tube	37 (53.6%)	47 (49.0%)	0.66
H_2 blocker	45 (65.2%)	59 (51.5%)	0.74
H^+ proton pump inhibitor	10 (14.5%)	32 (33.3%)	0.01

ICU: intensive care unit; SBT: skull-brain trauma; CVA: cerebral vascular accident; CHF: congestive heart failure; COPD: chronic obstructive pulmonary disease; APACHE II: Acute Physiology and Chronic Health Evaluation II.

Table 2 - Characteristics of the patients studied as a function of the antibiotics used, and duration of treatment according to implementation of the therapeutic guidelines. Londrina, Brazil, 2004.

Characteristic	Nonintervention (n = 69)	Intervention (n = 96)	p value
Previous use of antibiotics			
No	39 (56.5%)	42 (43.8%)	0.14
Yes	30 (43.5%)	54 (56.3%)	
Duration of previous use of antibiotics (days)			
1-5	19 (63.3%)	29 (53.7%)	0.68
6-10	6 (20.0%)	13 (24.1%)	
>10	5 (16.7%)	12 (22.2%)	
Antibiotics used for treatment			
Cefepime	53 (76.8%)	39 (40.6%)	0.00
Clindamycin	51 (73.9%)	7 (7.3%)	0.00
Vancomycin	35 (50.7%)	67 (69.8%)	0.02
Amikacin	32 (46.4%)	12 (12.5%)	0.00
Ceftriaxone	20 (29.0%)	1 (1.0%)	0.00
Imipenem	14 (20.3%)	23 (24.0%)	0.71
Meropenem	10 (14.5%)	22 (22.9%)	0.24
Metronidazole	10 (14.5%)	4 (4.2%)	0.03
Levofloxacin	4 (5.8%)	20 (20.8%)	0.01
Piperacillin/tazobactam	3 (4.3%)	48 (50.0%)	0.00
Ciprofloxacin	3 (4.3%)	6 (6.3%)	0.85
Chloramphenicol	1 (1.4%)	12 (12.5%)	0.02
Duration of treatment (days)	17.6 ± 15.8	16.6 ± 12.2	0.88
Stratified duration of treatment (days)			
≤7	19 (27.5%)	26 (27.1%)	0.93
8-14	18 (26.1%)	23 (24.0%)	
>14	32 (46.4%)	47 (49.0%)	

In the intervention period, 47 patients (49%) were discharged from the hospital (Table 3).

Discussion

In the present study, the implementation of therapeutic guidelines for the empirical treatment of nosocomial pneumonia reduced mortality in ICU patients. There were no reductions in treatment duration, ICU stay, or hospital stay. However, these results should be interpreted with caution. In studies evaluating two or more different periods, confounding variables can interfere with the results.[13] Such confounding variables include changes in medical and nursing staff, in the quality of invasive procedures, in the profile of in-hospital patients, in measures for prevention and control of cross infections, in the level of resistance of microorganisms, and in policies regarding the use of antimicrobial agents. Predisposing factors for pneumonia (age, comorbidities, MV, nasogastric tube, and drugs that change the gastric pH), as well as innovations in surgical techniques, can also be considered confounding variables.

Ventilator-associated pneumonia (VAP) is the most common and severe cross infection acquired in ICUs.[1,2] Among all cross infections, it is considered the main cause of death, ranging from 20 up to 70%. Mortality can be associated with comorbidities and not directly with pneumonia. However, this is a controversial issue and contradictory results have been reported.[14] The mortality rate is lower when the disease is caused by drug-sensitive bacteria. Among such bacteria, *P. aeruginosa* and *A. baumannii* have been associated with the worst prognosis.

The use of MV increases the risk of pneumonia by 6 to 21 times. As a consequence of this high

Table 3 - Patients with ICU-acquired pneumonia, according to length of ICU stay, length of hospital stay, and outcome. Londrina, Brazil, 2004.

Hospital stay (days)	Nonintervention (n = 69)	Intervention (n = 96)	p value
ICU stay (days)	18.7 ± 17.2	16.0 ± 12.2	0.66
Stratified ICU stay (days)			
1-10	29 (42.0%)	39 (40.6%)	0.71
11-20	20 (29.0%)	35 (36.5%)	
21-30	10 (14.5%)	10 (10.4%)	
>30	10 (14.5%)	12 (12.5%)	
Hospital stay (days)	32.0 ± 29.9	26.3 ± 17.3	0.49
Stratified hospital stay (days)			
1-10	14 (20.3%)	18 (18.8%)	0.36
11-20	17 (24.6%)	25 (26.0%)	
21-30	11 (15.9%)	25 (26.0%)	
>30	27 (39.1%)	28 (29.2%)	
Outcome			
Overall mortality	40 (57.9%)	49 (51.0%)	0.37
Pneumonia-related mortality	37 (53.6%)	25 (26.0%)	0.00

ICU: intensive care unit.

risk, most studies of pneumonia now focus on its association with this procedure.[1,15] In the present study, patients treated according to the therapeutic guidelines were more often placed on MV (p = 0.05). This could explain the isolation of multidrug-resistant bacteria. Most of the patients (74%) developed early pneumonia (within 4 days). Studies report that early pneumonia is common in patients with brain trauma.[16,17] It has also been reported that the most susceptible individuals are those infected with *S. aureus*,[18,19] with pulmonary aspiration,[20] or submitted to sedation.[17] In polytraumatized patients, the frequency of VAP ranges from 6 to 45%. Patients with acute cerebral vascular accident are considered to be at a high risk of acquiring pneumonia in the ICU, and intubation is one of the most influential factors.[21] In the present study, neurological alterations constituted the principal reason for ICU admission. The most frequent diagnoses for ICU admission were cranial trauma, cerebral vascular accident, and polytrauma. Therefore, these patients can be considered more susceptible to early pneumonia.

The profile of the bacteria isolated is more consistent with pneumonias acquired in a later phase, which can be partially explained by the fact that approximately half of the patients presented negative cultures due to the previous use of antibiotics. In the last ten years, changes in the microbiology of infections have been taking place, especially in terms of multidrug-resistance of hospital pathogens. The increase in the numbers of such microorganisms is primarily found in ICUs[1,22] as a result of the intense selective pressure imposed by the antibiotics used in these facilities. There is evidence that infections caused by multidrug-resistant pathogens have worse prognoses due to the delay in initiating the appropriate treatment. The *P. aeruginosa* and *A. baumannii* strains have become producers of cephalosporinases, which are resistant to piperacillin/tazobactam, aztreonam, and ceftazidime. *Klebsiella pneumoniae* and other enterobacteria are also becoming producers of extended-spectrum beta-lactamases, conferring resistance on third-generation cephalosporins.[23] Another multidrug-resistant, gram-negative bacillus is *S. maltophilia*, which was isolated in 11.5% of cultures of this study. In ICU patients, *S. aureus* is increasingly present, especially in those submitted to MV for a prolonged period. Therefore, the VAP microbiology is increasingly involving multidrug-resistant pathogens, posing difficulties to the treatment.[1,24]

The microorganisms found were the same in both periods. However, the frequency was lower in the nonintervention group, since there were fewer cultures performed in the nonintervention period. Although some authors have reported that tracheal

colonization by potentially pathogenic pathogens typically precedes pneumonia, this does not occur in all patients. Some authors[25,26] defend the hypothesis that when colonization by potentially resistant microorganisms (such as methicillin-resistant *S. aureus* or *K. pneumoniae*) that produce extended-spectrum beta-lactamases or other enterobacteria occurs, the risk of infection with these pathogens is high.

The number of days on MV and the administration of antibiotics before the development of pneumonia are independent risk factors associated with the development of pneumonia caused by multidrug-resistant microorganisms.[27] These facts could explain the presence of resistant strains in the present study, considering that 56.3% of the patients had previously been treated with antibiotics, and 83.3% had been submitted to MV before the development of infection. The presence of microorganisms that are resistant to antimicrobial agents is common in severe patients. Therefore, it is important that the first empirical treatment be broad-spectrum therapy.

Regarding the optimum period for treatment of nosocomial pneumonia, there is still no consensus. The use of antibiotics for a prolonged period has an effect on bacterial ecology and antibiotic toxicity, as well as increasing the cost of treatment. The treatment period proposed by the American Thoracic Society[10] is 14 days, or 21 days in the following situations, in which there is a risk of treatment failure: multilobar involvement; malnutrition; cavitation; necrotizing pneumonia; and pneumonia caused by *Acinetobacter* sp. or *P. aeruginosa*. When the pathogen is *S. aureus* or *Haemophilus influenzae*, the minimum period should be 7 to 10 days. It has been reported that shorter periods (8 days) are sufficient to treat VAP.[28] However, shorter treatment periods can increase the rate of recurrence, and longer periods of observation are therefore necessary. Short-duration treatment regimens are safe and can reduce the emergence of multidrug-resistant bacteria.[29] In the present study, there was no difference between the two groups in terms of treatment duration. This is likely attributable to the fact that, in both periods, the treatment duration was in compliance with the recommendation of the American Thoracic Society.[10]

For these reasons, strategies to improve the administration of antimicrobial agents, reduce bacterial resistance, and improve survival have been developed. The use of therapeutic guidelines is one alternative. In one study[27] carried out in two periods (before and after the implementation of therapeutic guidelines) and aimed at improving the use of antimicrobial agents, the authors did not observe differences in mortality rates. However, in the group treated according to the guidelines, the treatment was more effective ($p < 0.00$) and of a shorter duration ($p < 0.00$). In a recent publication, the American Thoracic Society[1] recommended the administration of early and appropriate antibiotic therapy as indispensable to avoid its excessive use, reducing the therapeutic spectrum when the etiology and the antibiogram allow it, as well as reducing the duration of treatment as much as possible.

Other authors[30] studied compliance with the protocol recommended by the Brazilian Consensus on Pneumonia[11] for the treatment of community-acquired pneumonias in elderly individuals. The authors found compliance with the protocol in 61.1% of the cases. Differences in the length of hospital stay, treatment costs, time to clinical stabilization, and index of severity of pneumonia were not observed between the two groups (those treated according to the consensus and those not treated according to the consensus). Regarding mortality, those with a higher index of severity (IV and V) presented higher mortality rates than did those who were not treated according to the consensus ($p = 0.04$).

There was, in the present study, ample compliance with the protocol, since the routine in this sector is to monitor patients closely and to follow the CCIH protocols in all patients being treated with antibiotic therapy.

Other studies have shown that a delay in initiating treatment increases mortality.[1,4,7] Therapeutic guidelines have been developed as an efficient means of avoiding the unnecessary use of antimicrobial agents and decreasing bacterial resistance. However, until now, few studies of the effects that implementing such guidelines has on mortality rates have been conducted. It is important to emphasize that every institution should establish its own protocol according to the prevalence and sensitivity patterns of the local microorganisms.

The results of the present study suggest that the implementation of therapeutic guidelines for the treatment of ICU-acquired pneumonia can be

effective in lowering the rates of pneumonia-related mortality. However, the implementation of the guidelines had no effect on treatment duration, time spent in the ICU, or the length of hospital stays.

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