ARTICLE

Effect of an Educational Intervention on the Management of Ventilator-Associated Pneumonia

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ABSTRACT

Background: The publication of guidelines for the management of ventilator-associated pneumonia prompted an evaluation of management of this condition in the intensive care unit (ICU) of a community acute care hospital.

Objectives: To evaluate the management of ventilator-associated pneumonia before and after an educational intervention for physicians and to determine the pathogens responsible for this condition among patients in this ICU.

Methods: The management of ventilator-associated pneumonia was reviewed, and compliance with published guidelines and with clinically appropriate therapy (in terms of subsequent culture results or local practice) was evaluated for the 7 months before and the 6 months after the 1-week educational intervention.

Results: A total of 42 episodes of ventilator-associated pneumonia, which occurred in 37 patients, were evaluated. After the educational intervention, the following changes in end points were observed: appropriate selection of empiric antibiotic therapy according to guidelines increased from 35% of episodes before to 59% of episodes after the intervention (p = 0.11), whereas the selection of empiric therapy subsequently deemed to be clinically appropriate increased from 45% to 77% (p = 0.032); appropriate dosing according to guidelines increased from 20% to 33% (p = 0.33), whereas clinically appropriate dosing increased from 70% to 95% (p = 0.027); appropriate route of therapy according to the guidelines increased from 75% to 82% (p = 0.59) but there was no change in clinically appropriate route of therapy (100% in both phases); timeliness of therapy increased from 85% to 91% (p = 0.56), de-escalation (narrowing of empiric therapy on the basis of culture results) increased from 60% to 100% (p = 0.11), and appropriate duration of therapy decreased from 79% to 55% (p = 0.11).

Conclusions: Clinically appropriate selection and dosing of antibiotics for ventilator-associated pneumonia improved after the educational intervention for physicians. The availability of local microbiological data was valuable in guiding empiric antibiotic selection.

RÉSUMÉ

Contexte : L'accessibilité aux lignes directrices en matière de traitement des cas de pneumonie sous ventilation assistée a incité une évaluation du traitement de ces cas dans une unité de soins intensifs d'un hôpital communautaire de soins de courte durée.

Objectifs : Évaluer le traitement des cas de pneumonie sous ventilation assistée avant et après une intervention formative auprès des médecins et identifier les agents pathogènes responsables de ces cas à l'unité de soins intensifs.

Méthodologie : Nous avons examiné le mode de traitement des cas de pneumonie sous ventilation assistée, la conformité aux lignes directrices publiées et la pertinence du traitement en fonction de la situation clinique (suivant les résultats de culture subséquents ou l'usage local) pendant sept mois avant l'intervention formative d'une semaine et pendant les six mois qui ont suivi.

Résultats : Nous avons évalué un total de 42 épisodes de pneumonie sous ventilation assistée chez 37 patients. Nous avons observé les changements suivants des critères d'évaluation après l'intervention : le choix de l'antibiothérapie empirique appropriée selon les lignes directrices a augmenté, passant de 35 % des épisodes avant l'intervention à 59 % des épisodes après l'intervention (p = 0,11), alors que le choix du traitement empirique jugé ultérieurement pertinent en fonction de la situation clinique a monté de 45 % à 77 % (p = 0,032); la posologie appropriée selon les lignes directrices a augmenté, passant de 20 % à 33 % (p = 0,33), tandis que la bonne posologie en fonction de la situation clinique a monté de 70 % à 95 % (p = 0,027); le choix de la voie de traitement appropriée selon les lignes directrices a augmenté, passant de 75 % à 82 % (p = 0,59), mais il n'y a eu aucun changement dans le pourcentage du choix de la bonne voie de traitement en fonction de la situation clinique (100 % dans les deux phases); l'opportunité du traitement a augmenté, passant de 85 % à 91 % (p = 0,56), de même que la désescalade (la restriction du traitement empirique suivant les résultats de culture), passant de 60 % à 100 % (p = 0,11); la durée appropriée du traitement a chuté de 79 % à 55 % (p = 0,11).

Conclusions : Il y a eu une amélioration dans le choix approprié du traitement en fonction de la situation clinique et

Key words: ventilator-associated pneumonia, guidelines, educational intervention

Can J Hosp Pharm 2008;61(4):256-263

dans la posologie des antibiotiques pour les cas de pneumonie sous ventilation assistée après l'intervention formative auprès des médecins. L'accès aux données microbiologiques locales a été d'une grande utilité pour guider le choix de l'antibiothérapie empirique.

Mots-clés : pneumonie sous ventilation assistée, lignes directrices, intervention formative

INTRODUCTION

Ventilator-associated pneumonia, defined as pneumonia that arises more than 48–72 h after endotracheal intubation, occurs in 9% to 27% of all patients who have been intubated.[1] This condition prolongs time on the ventilator and length of stay in the intensive care unit (ICU) and in the hospital after discharge from the ICU.[1] It accounts for approximately half of all infections in the ICU and is a major reason for the use of antibiotics in the ICU.[2] Previous studies have demonstrated that adequate empiric antibiotic therapy, as well as timely initiation of therapy, is associated with lower rates of in-hospital mortality and morbidity and lower costs.[3-6]

Publication of a set of guidelines for managing the care of adults with ventilator-associated and other types of pneumonia[1] prompted an evaluation of the management of ventilator-associated in the ICU at the authors' hospital. The guidelines provide recommendations on selection of empiric antibiotic therapy, as well as dosing, route of administration, timing, de-escalation according to culture results, and duration of therapy.[1] Because the guidelines' recommendations on empiric antibiotic therapy may not be applicable for local use, due to differences in local microbiological data, it was important to identify the types of bacterial pathogens associated with ventilator-associated pneumonia at our institution. An educational intervention was undertaken in which patient outcomes after management of ventilator-associated pneumonia in the ICU, along with targeted recommendations for improving management, were shared with ICU physicians. The objective of the study reported here was to evaluate the management of this type of pneumonia in the ICU before and after the intervention and to determine the local microbiologic data for ventilator-associated pneumonia in this ICU.

METHODS

ICU charts were reviewed to identify patients older than 18 years of age with a diagnosis of ventilator-associated pneumonia, which was defined as mechanical ventilation (continuous or intermittent) for a minimum of 48 h; new, worsening, or persistent infiltrate evident on chest radiography combined with 2 or more of the following criteria: fever (rectal temperature ≥38°C, oral temperature ≥37.5°C, or axillary temperature ≥37.0°C), leukocyte count ≥ 11 x 10^9/L or < 3.5 x 10^9/L, purulent endotracheal secretions, increasing oxygen requirements, or positive results on culture of endotracheal aspirate obtained within the preceding 48 h.[7] Each episode of ventilator-associated pneumonia during a patient's ICU stay was evaluated to characterize both early-onset and late-onset episodes and the pathogens responsible for each type. A second episode was considered to have occurred if it was diagnosed at least 48 h after completion of the course of antibiotic treatment for the first episode.[5] There were no specific exclusion criteria.

The ICU where the study was conducted is a 9-bed medical–surgical unit in a community acute care hospital that is staffed by attending physicians only; the hospital has clinical pharmacy services but no infectious diseases service. Ethics approval was granted by the University of British Columbia Clinical Research Ethics Board.

In phase 1 of this study we evaluated the management of ventilator-associated pneumonia for eligible patients admitted over a 7-month period (April 1, 2006, to October 31, 2006). Over the 1-week period from November 1 to 7, 2006, 2 of the investigators (Z.K., S.G.) conducted a verbal educational intervention with each of the 5 ICU physicians; the verbal component was supplemented by written information summarizing the findings from the phase 1 evaluation and outlining targeted recommendations for improving the selection, dosing, de-escalation, and duration of empiric antibiotic therapy, based on the phase 1 findings. During phase 2 of the study, we evaluated the management of ventilator-associated pneumonia after the intervention; this phase included eligible patients admitted over the 6-month period from November 7, 2006, to April 30, 2007. Data collected during the 2 phases included pathogens identified from culture of sputum and

blood, and the selection, dosing, route, timeliness, de-escalation, and duration of empiric antibiotic therapy for each episode of ventilator-associated pneumonia.

Two methods were used to evaluate the appropriateness of empiric therapy: comparison with the published guidelines[1] and evaluation of clinical appropriateness in terms of subsequently available culture results. The published guidelines recommend empiric therapy according to the following situations: diagnosis of early-onset ventilator-associated pneumonia (within 4 days of admission to hospital) and no risk factors for multidrug-resistant pathogens, diagnosis of late-onset ventilator-associated pneumonia (5 days or more after admission), or presence of risk factors for multidrug-resistant pathogens (Table 1).[1] For patients with early-onset pneumonia and no risk factors, the guidelines recommend ceftriaxone, levofloxacin, moxifloxacin, ciprofloxacin, ampicillin–sulbactam, or ertapenem as empiric antibiotic therapy. For patients with late-onset ventilator-associated pneumonia or risk factors for multidrug-resistant pathogens, the guidelines recommend an antipseudomonal cephalosporin (cefepime or ceftazidime) or an antipseudomonal carbapenem (imipenem or meropenem) or a ß-lactam/ß-lactamase inhibitor (piperacillin–tazobactam) plus either an antipseudomonal fluoroquinolone (ciprofloxacin or levofloxacin) or an aminoglycoside (amikacin, gentamicin, or tobramycin). In addition, linezolid or vancomycin is recommended for methicillin-resistant *Staphylococcus aureus* (MRSA) if risk factors for this organism are present or there is a high incidence of MRSA locally.[1] Of the antibiotics recommended in the guidelines, those on the hospital's formulary at the time of the study included cefotaxime in place of ceftriaxone, moxifloxacin, ciprofloxacin, ceftazidime, meropenem, piperacillin–tazobactam, gentamicin, and vancomycin. Although the incidence of MRSA at this institution was not known and an antibiogram had not been published for a few years, the incidence of MRSA was anecdotally considered to be low, and the empiric addition of vancomycin or linezolid was not deemed necessary. Therapy was considered clinically appropriate if the antibiotics selected empirically were subsequently found to be effective against the pathogen(s) identified, based on susceptibility reporting in the culture results.

Two methods were also used to evaluate dosing. First, empiric dosing for agents available at this institution was compared with the dosing recommended in the guidelines (ceftazidime 2 g q8h, meropenem 1 g q8h, piperacillin–tazobactam 4.5 g q6h, gentamicin 7 mg/kg per day, ciprofloxacin 400 mg q8h, and vancomycin 15 mg/kg q12h). Then, empiric dosing was compared with dosing considered clinically appropriate on the basis of practice at local hospitals; these locally accepted dosing practices did not have an evidentiary basis. Regimens considered clinically appropriate that were different from those recommended in the guidelines included ciprofloxacin 400 mg q12h and, for patients with body weight less than 100 kg, cefotaxime and ceftazidime 1 g q8h and piperacillin–tazobactam 3.375 g q6h. Dosing adjustments for renal dysfunction were considered in evaluating the appropriateness of dosing.

The guidelines defined IV therapy as the only appropriate empiric route of therapy; however, oral therapy was considered clinically appropriate if the patient was hemodynamically stable (not requiring vasopressor therapy) and was able to tolerate oral or nasogastric feeding and antibiotics with good oral bioavailability (i.e., ciprofloxacin) were being used.

Therapy was considered timely if it was initiated within 24 h after diagnosis of ventilator-associated pneumonia.

Table 1. Risk Factors for Multidrug-Resistant Pathogens Causing Hospital-Acquired, Health-Care-Associated, and Ventilator-Associated Pneumonia[1]

Antimicrobial therapy in preceding 90 days
Current hospital stay of 5 days or more
High frequency of antibiotic resistance in the community or in the specific hospital unit
Presence of risk factors for health-care-associated pneumonia:
Hospital stay for 2 days or more in the preceding 90 days
Residence in a nursing home or extended care facility
Home infusion therapy (including antibiotics)
Long-term dialysis within the preceding 30 days
Home wound care
Family member with multidrug-resistant pathogen
Immunosuppressive disease and/or therapy

Table 2. Demographic Characteristics of Patients

Characteristic	Mean ± SD*	
	Phase 1 (*n* = 17)	Phase 2 (*n* = 20)
Sex (no. and % men)	13 (76)	14 (70)
Age (years)	57 ± 17	53 ± 18
Weight (kg)	86 ± 21	91 ± 38
APACHE II score	25 ± 6	21 ± 9
Duration of mechanical ventilation (days)	25 ± 21	17 ± 12
Length of stay in ICU (days)	29 ± 24	19 ± 13
Hospital length of stay (days)	43 ± 43	25 ± 13
No. (%) of deaths in ICU	4 (24)	2 (10)
No. (%) of patients with risk factors for multidrug-resistant pneumonia	14 (82)	16 (80)
No. (%) of patients with immunodeficiency	2 (12)	0

SD = standard deviation, APACHE = Acute Physiology and Chronic Health Evaluation, ICU = intensive care unit.
*Unless indicated otherwise.

De-escalation (narrowing of therapy on the basis of culture data) was considered appropriate if the therapy was narrowed within 24 h after positive culture results became available. In addition, therapy could be de-escalated if patients had no other potential concurrent sources of infection that might have required therapy.[5]

Appropriate duration of therapy was defined as 7 days ± 1 day unless *Pseudomonas aeruginosa* or *Acinetobacter* sp. was cultured, in which case the appropriate duration of therapy was defined as 14 days ± 1 day, or unless the patient was immunocompromised, had bacteremia, or had persistent signs and symptoms consistent with active infection, in which case it was appropriate to continue therapy until clinical resolution.[1,2,5]

The results from phases 1 and 2 were compared using the χ^2 test. Data were analyzed using the QuickCalcs Online Calculator for Scientists (GraphPad Software). A p value less than 0.05 was deemed significant.

RESULTS

A total of 37 patients were included in the study: 17 during phase 1 and 20 during phase 2 (Table 2). A total of 42 episodes of ventilator-associated pneumonia occurred: 20 (48%) during phase 1 and 22 (52%) during phase 2. Five (12%) of the 42 episodes were second episodes in patients who had completed a course of therapy for an earlier episode. Late-onset episodes were more common than early-onset episodes (29 [69%] and 13 [31%], respectively).

The pathogens responsible for early- and late-onset ventilator-associated pneumonia at this institution over the entire 13-month period of the study are shown in Figure 1. MRSA was isolated in 4 (10%) of the 42 episodes, occurring primarily in patients with risk factors for MRSA, including injection drug use (2 episodes), homelessness (1 episode), and prolonged hospital stay (i.e., longer than 1 month) (1 episode). In 31% (9/29) of late-onset episodes of ventilator-associated pneumonia and 37% (11/30) of episodes in patients with risk factors for multidrug-resistance, organisms were isolated for which combination therapy might have been warranted to prevent emergence of resistance.

Table 3 summarizes the appropriateness of selection, dosing, route, and duration of therapy, as well as the timeliness of initiation of therapy.

De-escalation of therapy was not possible in 32 (76%) of the 42 episodes of ventilator-associated pneumonia, for the following reasons: de-escalation would have been inappropriate, given the pathogens identified (16 episodes [50%]); therapy had been initiated on the basis of the culture results, so de-escalation did not apply (8 episodes [25%]); culture results were negative (4 episodes [12%]); and there were other potential sources of infection (4 episodes [12%]). Of the 10 episodes (5 in each phase) that were eligible for de-escalation, appropriate de-escalation of therapy increased from 60% (3/5 episodes) before to 100% (all 5 episodes) after the intervention (p = 0.11).

Among patients who should have received a 7-day course of therapy, the proportion whose duration of therapy was appropriate increased from 67% (6/9 episodes) in phase 1 to 43% (6/14 episodes) in phase 2 (p = 0.27). Among episodes for which an extended duration of therapy was warranted because of growth of *Pseudomonas* or *Acinetobacter* or because of persistent signs and symptoms of infection, bacteremia, or immunocompromise, the proportion decreased from

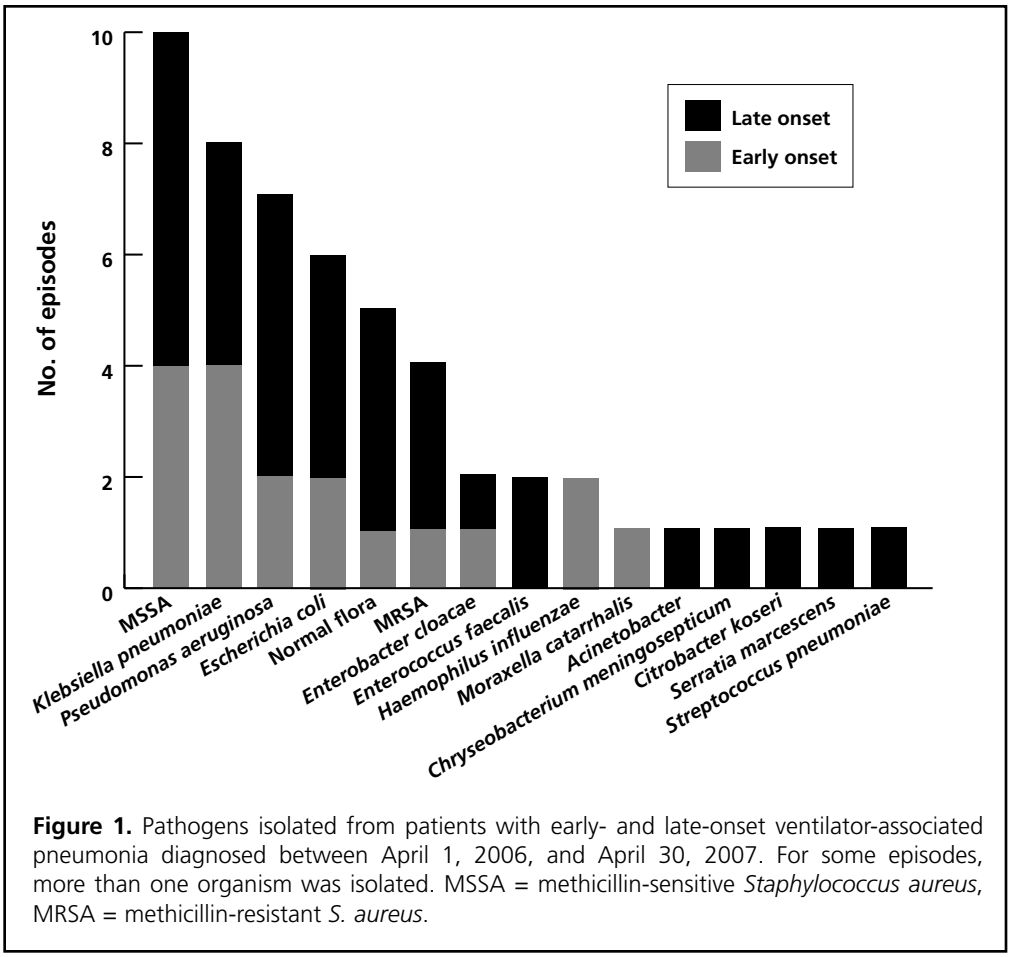

Figure 1. Pathogens isolated from patients with early- and late-onset ventilator-associated pneumonia diagnosed between April 1, 2006, and April 30, 2007. For some episodes, more than one organism was isolated. MSSA = methicillin-sensitive *Staphylococcus aureus*, MRSA = methicillin-resistant *S. aureus*.

90% (9/10) to 83% (5/6) (p = 0.70). The mean (min, max) duration of therapy overall appeared to improve after the educational intervention: from 12 days (7, 22) to 10 days (6, 15); the mean duration of therapy also seemed to improve for patients who required an extended course of therapy: from 15 (10, 22) days to 12 (8, 15) days. There was no change in the mean duration of therapy for patients who required a 7-day course of therapy (9 days in both phases).

DISCUSSION

The results of the study reported here indicate that the management of ventilator-associated management improved in a number of ways after the educational intervention, although only the clinically appropriate selection and dosing of antibiotics reached statistical significance. Previous studies have also demonstrated the effectiveness of educational interventions. Serisier and others[8] found that a simple, inexpensive educational intervention was associated with significant improvements in the hospital management of community-acquired pneumonia, specifically in terms of 2 end points that had been shown to influence outcomes: median time to IV administration of antibiotics and rate of prescription of macrolide antibiotics.

The availability of local microbiological data likely played an important role in improvements in the use of double antibiotic coverage for patients with late-onset pneumonia and risk factors for multidrug-resistant pathogens. According to these local findings, 31% of the pathogens isolated from patients with late-onset pneumonia and 37% of those from patients with risk factors for multidrug-resistant pathogens were organisms that might warrant combination therapy to prevent emergence of resistance; therefore, the guideline recommendations to empirically use combination therapy for these 2 groups of patients seems reasonable. The finding of a relatively low incidence of MRSA as a causative pathogen for ventilation-associated pneumonia at this institution reinforces the hospital's practice of not routinely using linezolid or vancomycin for the empiric treatment of all late-onset episodes or for all patients with risk factors for multidrug-resistant pathogens. Instead, our institution

Table 3. Appropriateness of Aspects of Empiric Antibiotic Therapy for Ventilator-Associated Pneumonia

Criterion	No. (%) of Episodes of Ventilator-Associated Pneumonia		*p* value
	Phase 1 (*n* = 20)	Phase 2 (*n* = 22)	
Appropriate selection			
According to guidelines	7 (35)	13 (59)	0.11
According to local clinical practice	9 (45)	17 (77)	0.032
Appropriate dosing			
According to guidelines	4 (20)	7 (33)*	0.33
According to local clinical practice	14 (70)	21 (95)	0.027
Appropriate route			
According to guidelines	15 (75)	18 (82)	0.59
According to local clinical practice	20 (100)	22 (100)	>0.99
Timeliness	17 (85)	20 (91)	0.56
Appropriate duration	15 (79)†	11 (55)‡	0.11

*Percentage calculated with a denominator of 21 because cefuroxime, which is not included in the guidelines, was used on the basis of culture results.
†Percentage calculated with a denominator of 19 because one patient died while receiving antibiotics.
‡Percentage calculated with a denominator of 20 because 2 patients died while receiving antibiotics.

uses a targeted approach of treating patients with risk factors for MRSA such as prior MRSA infection, stay in a nursing home, homelessness, and injection or other drug use.[9] This illustrates the importance of knowing local microbiological patterns of infection when applying clinical guidelines in practice.

The main reasons for designation of empiric therapy as inappropriate were lack of use of a combination empiric regimen for patients with late-onset ventilator-associated pneumonia or risk factors for multidrug-resistant pathogens, and use of an agent inappropriate for early-onset episodes (e.g., cefuroxime or clindamycin).

The main reasons for designation of dosing as inappropriate relative to the guidelines were underdosing of piperacillin–tazobactam (3.375 g rather than 4.5 g), ciprofloxacin (q12h rather than q8h), meropenem (500 mg rather than 1000 mg), and third-generation cephalosporins (1 g rather than 2 g). Reasons for designation of dosing as clinically inappropriate were underdosing of meropenem (500 mg rather than 1000 mg) and third-generation cephalosporins (use of 1 g for patients with body weight greater than 100 kg). We evaluated the clinical appropriateness of dosing in this study because some of the dosing regimens used at this institution and other local institutions differ from recommendations in the guidelines. Studies of meropenem have all used doses of 1 g every 8 h.[10,11] The institution's original practice of giving meropenem 500 mg every 8 h was not evidence-based, nor was this regimen used by other local institutions; this practice was therefore discouraged during the educational intervention. Although studies assessing ciprofloxacin in ventilator-associated pneumonia have typically used doses of 400 mg IV every 8 h, this drug is usually given every 12 h in clinical practice at this and many other institutions, and use of every 12 h dosing continues at our institution.[12] In patients with severe infections, 2-g doses of third-generation cephalosporins are usually recommended; however, the practice of using 1 g of these drugs for patients weighing less than 100 kg is reasonable; it has been used in practice without clinical failures[13,14] and continues at our institution. After the educational intervention, more patients with body weight above 100 kg appropriately received 2-g doses of third-generation cephalosporins.

The appropriateness of route of therapy relative to the guideline recommendations remained essentially unchanged after the educational intervention because agents with good oral bioavailability, such as ciprofloxacin, continued to be given orally to patients who were clinically stable and able to tolerate oral or nasogastric feeding, even though the guidelines advocated only IV therapy. Although we could not find any studies that had evaluated the use of empiric oral therapy in the critically ill population, patients in the ICU who are hemodynamically stable and are tolerating oral or nasogastric feeding may be adequately treated empirically with oral antibiotics having good bioavailability. This topic deserves further evaluation.

Antibiotics were being administered in a timely manner before the educational intervention, but this practice showed some improvement after the intervention. The data describing an improvement in

de-escalation of therapy were limited by the small number of patients who were eligible for de-escalation.

The reasons for a lack of improvement in appropriate duration of therapy were difficult to determine because of the retrospective nature of the study. Despite the lack of improvement in the proportion of patients receiving an appropriate duration of therapy after the educational intervention, the overall mean duration of therapy did improve. Even so, the mean duration of therapy after the intervention was still longer than that considered appropriate according to the guidelines. More specifically, the duration of therapy was longer by an average of 2 days for patients who should have received a 7-day course of therapy. In a randomized controlled trial, Chastre and others[15] found no difference in mortality among patients with microbiologically proven ventilator-associated pneumonia treated for 8 and 15 days. However, they did find a higher rate of recurrence of pulmonary infection among patients with gram-negative bacilli such as *Pseudomonas* who were treated for 8 days relative to those treated for 15 days (40.6% vs. 25.4%; difference 15.2 percentage points, 90% confidence interval 3.9–26.6 percentage points). Therefore, the practice of treating patients with ventilator-associated pneumonia caused by gram-negative bacilli such as *Pseudomonas* and *Acinetobacter* for 14 days, which is common in clinical practice and which was considered clinically appropriate in our study, appears reasonable.

Although there were many aspects of the management of ventilator-associated pneumonia that seemed to improve after the educational intervention, there is room for further improvement. A single educational intervention, without incorporation of an active intervention, is unlikely to be sufficient to maintain the improvements seen in this study, and the duration of the impact of our intervention is unknown. In addition, despite face-to-face interaction with each of the 5 ICU physicians, the 1-week period during which the intervention took place may not have been an adequate adjustment period.

The strengths of this study included defining end points in terms of both published guidelines and local clinical practice where applicable, which provided potentially more relevant data, and identifying local pathogens responsible for ventilator-associated pneumonia. The limitations of the study included its retrospective design and small sample size. In addition, antibiotics may be used in critically ill patients for unknown sources of infection or for more than one possible source of infection; therefore, it may be difficult in a retrospective study to isolate therapy used for ventilator-associated pneumonia from therapy for other infections, particularly for end points such as selection of empiric therapy, de-escalation, and duration of therapy.

There was a significant improvement in the clinically appropriate selection and dosing of antibiotics for ventilator-associated pneumonia after the educational intervention. Additional aspects of therapy, such as selection and dosing of empiric antibiotic therapy in accordance with guidelines and the timeliness and de-escalation of therapy also seemed to improve, although the changes did not reach statistical significance. The availability of local microbiological data was valuable in guiding empiric antibiotic selection for the management of this condition at our institution.

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