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Major article

Trends in ventilator-associated pneumonia: Impact of a ventilator care bundle in an Italian tertiary care hospital intensive care unit

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Background: The impact on ventilator-associated pneumonia (VAP) occurrence of a multifaceted program, including progressive strategies for VAP prevention, implemented in an Italian intensive care unit (ICU) is reported.

Methods: All adults admitted to the ICU in 2004-2010 with a length of stay ≥72 hours and mechanical ventilation time ≥48 hours were included in the study. Demographics, clinical information, and data on VAP were extracted from the ICU-acquired infection surveillance dataset. A standardized bundle for VAP prevention was implemented in 2004. In 2008, selective digestive tract decontamination (SDD) was added to the protocol. Changes in VAP incidence were evaluated.

Results: There were 1,372 subjects included in the study. Overall, 156 (11.4%) developed VAP. In the second part of the study VAP incidence decreased from 15.9% to 6.7% ($P < .001$). Reductions both in early-onset VAP (6.6% to 1.9%; $P < .001$) and late-onset VAP (9.3% to 4.7%; $P = .001$) incidence were observed. Multivariate analysis showed a significant reduction in the risk of developing VAP from multidrug-resistant pathogens in the bundle plus SDD period as well (odds ratio, .54; 95% confidence interval, .31-.91).

Conclusion: The implementation of a standardized approach to patient care, including a number of key reduction interventions, was associated with a significant reduction in the risk of developing VAP.

Ventilator-associated pneumonia (VAP) is a major hospital-acquired infection in patients admitted in an intensive care unit (ICU) with a risk of developing pneumonia. It depends on patient's comorbidities, clinical status, and length of mechanical ventilation (MV).[1] Patients developing VAP have higher mortality rates, longer ICU and hospital stays, and higher health care–associated costs compared with patients without VAP. Therefore, prevention and surveillance of respiratory tract infections have been recognized as crucial points for improving the outcome of critically ill patients admitted in an ICU.[2]

Both general strategies for infection control (eg, staff education, adherence to hand hygiene rigorous protocols) and specific strategies to prevent aspiration, reduce colonization of the aerodigestive tract, and minimize contamination of equipment are currently recommended by evidence-based guidelines for VAP prevention.[3-6] In recent years, to improve implementation of guidelines, different sets of key procedures (ventilator care bundles) have been proposed and included in clinical protocols for prevention.[7,8] However, the impact of these measures in real clinical life on VAP occurrence remain to be well defined.[9,10]

The impact on the risk of developing VAP and on patients' outcomes of a multifaceted program, including progressive targeted strategies for prevention of VAP, which has been implemented in the ICU of a tertiary care hospital in Northern Italy, are reported.

METHODS

Patients and setting

In this retrospective observational analysis we studied all the adult patients with an ICU length of stay (LOS) ≥72 hours and

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receiving MV ≥48 hours admitted from January 2004-December 2010, to the ICU of the University Hospital of Modena, a 700-bed tertiary hospital in Northern Italy. The 10-bed ICU has around 800 admissions per year. During the study period the mean LOS was 3.5 days, and approximately 45% of the patients received MV.

VAP prevention protocol

In September 2003, a multidisciplinary group developed a clinical protocol for VAP prevention and defined the strategies for favoring its implementation in clinical practice.

The initial protocol (VAP preventive bundle) included a set of interventions indicated by published guidelines: (1) careful hand hygiene according to hospital protocol for handwashing; (2) keeping patients in a 30° semirecumbent position; (3) endotracheal cuff pressure ≥20 cm H_2O; (4) oral care with chlorhexidine 0.12% at least 2 times a day in ventilated patients; (5) avoiding gastric overdistension and withdrawal of enteral nutrition 2 hours before nursing and patient transport to reduce the risk of aspiration; (6) avoiding programmed tracheal suction and use of closed endotracheal suctioning system when possible; (7) substitution of heat and moisture changers and ventilator circuits every 72 hours and 7 days, respectively, or when visibly soiled; and (8) daily assessment of readiness to weaning or extubation.

These VAP prevention items were applied throughout the study period without substantial changes. However, toward the end of 2007, a selective digestive tract decontamination (SDD) for patients with a predicted ventilation period >48 hours was introduced in the VAP prevention protocol (VAP preventive bundle plus SDD). The SDD regimen consisted of a 3 times per day topical application of tobramycin, colistin, and amphotericin B in the oropharynx and stomach plus a 4-day course of intravenous cefotaxime in patients without wide-spectrum antibiotic therapy for other reasons.

Orotracheal intubation was used in all patients. Continuous subglottic aspiration was never used. Stress ulcer prophylaxis and sedation were managed according to local protocols that did not substantially change in the study period.

VAP definitions

VAP was defined as (1) the presence of a new persistent infiltrate observed at chest radiograph or computed tomography scan at least 48 hours after orotracheal intubation associated with at least one of the following: worsening of oxygenation, purulent bronchial secretions, leukocytosis, and fever; and (2) the presence of potentially pathogenic microorganisms in culture from tracheal aspirate and bronchoalveolar lavage with $\geq 10^6$ and $\geq 10^4$ colony forming units, respectively. Early-onset VAP (EVAP) was defined as occurring within 96 hours of MV, or late-onset VAP (LVAP) occurred later. Multidrug-resistant (MDR) bacteria were defined on the basis of the antibiotic resistance pattern as follows: *Staphylococcus aureus* with methicillin resistance; Enterococcus spp resistant to glycopeptides; *Enterobacter* spp resistant to fluoroquinolons or carbapenems or extended spectrum β-lactamase producers; *Pseudomonas* spp and *Burkholderia cepacia* resistant to carbapenems or piperacillin-tazobactam; and *Acinetobacter baumannii* sensitive to colistin and tigecycline only. *Stenotrophomonas maltophilia* was always considered as an MDR bacteria for its intrinsic resistance to antibiotics.

Data collection

Since 2002, the ICU has been participating in the Italian Group for the Evaluation of Interventions in Intensive Care Medicine (GiViTI) project Margherita, which promotes research and data collection in ICUs for the continuous quality of care assessment and improvement: it now involves >150 Italian ICUs.[11] A specific set of data is collected in a prospective way for all patients admitted in the ICU by a dedicated and trained team in accordance with the guidelines and definitions of the national protocol. Data include demographics, admission diagnoses, comorbidities, reasons for admission, Simplified Acute Physiology Score II (SAPS II), major procedures and interventions during the stay, and ICU and hospital outcomes. For all patients with infection, the following data are also collected: date of occurrence, microorganisms with their sensitivity patterns, multiple episodes, origin of infection, and severity reached. Numerous validity checks about consistency, plausibility, and completeness of data have been set up and are routinely carried out both by the coordinating center and by each participating unit. In this ICU, data are checked each semester by a dedicated multidisciplinary group, and microbiological information is routinely verified by comparing data with the microbiology laboratory database: sufficiently high accuracy and completeness of data (according to surveillance protocol, valid data for >90% of patients each surveillance month) were reached at the end of 2003.

For the purpose of this specific study, data have been extracted from this dataset, and further not previously validated information was not added.

Statistical analyses

Cumulative incidence of VAP was expressed as the proportion of patients with VAP among subjects included in the study. Only the first episode of VAP was considered. VAP incidence referred to 2 different study periods: VAP preventive bundle period (2004-2007) and VAP preventive bundle plus SDD period (2008-2010). VAP incidence, VAP risk factor prevalence at ICU admittance, and patient outcomes were compared by analysis of variance or Student *t* test for continuous variables and Pearson χ^2 test or Fisher exact test for categorical variables. Changes in VAP risk were further investigated using multivariate logistic regression analysis: odds ratios and 95% confidence intervals were estimated by adjusting for potential confounders (age, type of admission, SAPS II at ICU admittance). Two-tailed $P < .05$ was considered to be statistically significant. Data were analyzed using SPSS version 20 (SPSS Inc, Chicago, IL).

RESULTS

In the study period, 1,372 patients admitted to the ICU had an ICU LOS ≥72 hours and a MV time ≥48 hours and therefore were eligible for our study. Overall, 156 subjects (11.4%) developed VAP: LVAP accounted for 62.3% of VAP cases (n = 97 cases, 7.1% of patients), whereas 59 subjects (4.3% of patients) developed EVAP (37.7% of VAP cases). The most commonly isolated organisms were Enterobacteriaceae (32.9%) followed by *Pseudomonas* spp, including *B cepacia* (30.1%), *S aureus* (14.1%), and Enterococci (8.2%). In 69 infections (44.2% of VAPs, 5.0% of patients), MDR bacteria were isolated. Three major epidemics occurred during the study period: an outbreak of MDR *P aeruginosa* and one caused by *B cepacia* started in 2005, and an epidemic caused by MDR *A baumannii* occurred in 2009. Excluding these epidemic episodes, VAP caused by MDR pathogens was sustained mainly by methicillin-resistant *S aureus* (23.2% of VAP from MDR microorganisms), Enterobacteriaceae (20.9%), and Enterococci (12.8%).

Patients with VAP had significantly higher SAPS II at ICU admittance ($P = .017$), longer duration of MV ($P < .001$), longer ICU