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EDITORIAL

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Prevention of VAP: the whole is more than the sum of its parts

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"The whole is more than the sum of its parts."

Aristotle

Nosocomial infections are by far the most common complications affecting hospitalized patients [1]. Ventilator-associated pneumonia (VAP) is the most frequent infectious complication in ICU patients, increasing costs by more than U$ 40,000 per patient [2]. The most effective treatment is prevention. Currently, infection control is a critical element of patient care and every nosocomial infection is considered potentially preventable. Performing a root-cause analysis to evaluate factors that contribute to infection development might allow identification of potential interventions for prevention [3]. In the USA, the Centers for Medicare and Medicaid Services plan to stop paying hospitals for care made necessary by preventable complications [4], including nosocomial infections, which may have both desirable and unintended consequences. Eight preventable complications will no longer be reimbursable as of October 2008, including two that occur in ICUs, vascular-catheter-associated infection and catheter-associated urinary tract infection. Other ICU infections may follow, such as VAP and methicillin-resistant *Staphylococcus aureus* (MRSA) infection. This underscores the need to implement effective prevention strategies. The plan has been criticized for penalizing hospitals that admit frail and other high-risk patients [5]. In addition, the plan may inadvertently encourage institutions to underreport nosocomial infections. Ideally, payment should be based on implementation of prevention strategies and demonstration of improvement by active surveillance.

Additionally, it is important to recognize that adequate nursing and respiratory therapy staffing levels may influence the duration of stay of patients in intensive care units and the development of VAP, presumably due to maintenance of infection control standards [6, 7]. Lapses in basic infection control measures like handwashing and patient isolation for multidrug-resistant pathogens are more likely with increased workloads for registered nurses and increased reliance on less trained health-care personnel to deliver care [8–10]. The duration of mechanical ventilation can also be reduced by appropriate staffing levels in the ICU, which may also influence the development of VAP [11, 12]. Educational reinforcement and opportunities for ICU staff to participate in mandatory training aimed at HAP/VAP prevention is also important in preventing VAP [13, 14]. Unfortunately, many ICUs may have staffing problems, which limits the overall success of infection control measures that are dependent on active intervention by the bedside nurse [8, 10].

Several isolated interventions have demonstrated a reduction in the incidence of VAP [15]. The endotracheal tube is a major risk factor for the occurrence of VAP. Prevention measures targeting the endotracheal tube aim to minimize tube colonization and formation of biofilm

(e.g. use of antimicrobial-coated tubes) and avoidance of microaspiration (e.g. aspiration of subglottic secretions and control of intracuff pressure). The presence of the endotracheal tube breaches first-line defense mechanisms, providing airway access to both liquefied and aerosolized particles [16]. Biofilm formation in the inner surface of the endotracheal tube provides a protected environment for pathogens that are less susceptible to killing by host defenses. Moreover, biofilm can detach, dislodging biofilm-encased bacteria contaminating the airway, and it might increase the risk of late-onset pneumonia. Prevention of bacterial biofilm formation might avoid colonization, a precursor of VAP [15].

In this issue of *Intensive Care Medicine*, Berra et al. [17] describe an experimental model with antimicrobial-coated endotracheal tube (silver-sulfadiazine). After in vitro challenge every 24 h with 10^4–10^6 *Pseudomonas aeruginosa*/ml the antibacterial-coated endotracheal tube (ET) remained bacteria-free up to 72 h, whereas the standard ET showed heavy *P. aeruginosa* growth and biofilm formation. Moreover, in an in vivo experiment, a sheep model mechanically ventilated for 24 h, the antibacterial coated ET showed no bacterial growth in the inner surface of the ET, ventilator tubing and lower respiratory tract, whereas standard ET group developed heavy colonization in all these sites [18]. The main limitations of this study are assessment of colonization only by *P. aeruginosa* and the limited duration of the animal study. As colonization by *P. aeruginosa* is associated more significantly with late-onset VAP, 24 h of mechanical ventilation is a too short period to evaluate prevention of colonization.

The covering of biomedical devices with silver for the prevention of nosocomial infections is based on its broad-spectrum antimicrobial activity [19], reduction of bacterial adhesion [20] and blockage of biofilm formation [21]. It has been evaluated clinically in urinary catheters for prevention of urinary infection, with positive results [22], and experimentally in ET [23, 24]. Rello et al. [25] assessed the feasibility and safety of a silver-coated ET in a phase II randomized controlled trial and found that the device was well tolerated and associated with reduced and delayed bacterial colonization of airway secretions as well as the surface of the tube. A phase III multicenter, prospective, randomized, controlled trial demonstrated a significant reduction of microbiologically documented VAP (4.8% in the silver group vs 7.5% in the control group, $p < 0.05$) [26]. This has led to the availability of the first commercially available silver-coated ET in the USA (FDA News, 8 November 2007).

Application of evidence-based interventions is highly variable with low overall adherence to current recommendations [27]. The new paradigm of nosocomial infection prevention should be based on an organized, multidisciplinary, and evidence-based effort with an agenda focused on patient safety promotion and quality improvement. The cornerstone of this approach is the Institute for Health Improvement (IHI) initiative that incorporates a limited number of effective interventions in a bundle, conceptually simple and feasible. Prevention based in a care bundle aims to translate the best available evidence to clinical practice, allowing a more uniform management of the patient. Whereas implementation of individual interventions might improve patient care, the simultaneous implementation of several simple measures simultaneously, as a care bundle has a greater likelihood of improving outcome [28, 29]. Furthermore, this format allows a more effective implementation of the prevention strategy. Resar et al. [28] found a reduction of 45% in VAP incidence with the implementation of a care bundle for VAP prevention. Moreover, reduction in VAP incidence is correlated to the degree of adherence to the bundle. Again it is important to note that successful compliance with infection control bundles will depend on having adequate and well-educated staffing in the ICU. A benefit of the silver-coated ET is that it is not dependent on staffing conditions and will provide protection even when other prevention practices are not applied.

New devices or newly developed prevention interventions should be evaluated under this new paradigm as part of a coordinated strategy for nosocomial infection prevention. Incorporation of new techniques in bundles with feasible evidence-based measures seems to be the easiest way to get compliance and to optimize VAP prevention.

References

1. Burke JP (2003) Infection control: a problem for patient safety. N Engl J Med 348:651–656
2. Rello J, Ollendorf DA, Oster G, Vera-Llonch M, Bellm L, Redman R, Kollef MH (2002) Epidemiology and outcomes of ventilator-associated pneumonia in a large US database. Chest 122:2115–2121
3. Gerberding JL (2002) Hospital-onset infections: A patient safety issue. Ann Intern Med 137:665–670
4. Edwards JR, Peterson KD, Andrus ML, Tolson JS, Goulding JS, Dudeck MA, Mincey RB, Pollock DA, Horan TC, NHSN Facilities (2007) National Healthcare Safety Network (NHSN) Report, data summary for 2006. Am J Infect Control 35:290–301
5. Rosenthal MB (2007) Nonpayment for performance? Medicare's new reimbursement rule. N Engl J Med 357:1573–1575
6. Needleman J, Buerhaus P, Mattke S, Stewart M, Zelevinsky K (2002) Nurse staffing levels and the quality of care in hospitals. N Engl J Med 346:1715–1722

7. Cho SH, Ketefian S, Barkauskas VH, Smith DG (2003) The effects of nurse staffing on adverse events, morbidity, mortality and medical costs. Nursing Res 52:71–79
8. Archibald LK, Manning ML, Bell LM, Banerjee S, Jarvis WR (1997) Patient density, nurse-to-patient ratio and nosocomial infection risk in a pediatric cardiac intensive care unit. Pediatr Infect Dis J 16:1045–1048
9. Fridkin SK, Pear SM, Williamson TH, Galgiani JN, Jarvis WR (1996) The role of understaffing in central venous catheter-associated bloodstream infections. Infect Control Hosp Epidemiol 17:150–158
10. Pittet D, Mourouga P, Perneger TV (1999) Compliance with handwashing in a teaching hospital. Ann Intern Med 130:126–130
11. Thorens JB, Kaelin RM, Jolliet P, Chevrolet JC (1995) Influence of the quality of nursing on the duration of weaning from mechanical ventilation in patients with chronic obstructive pulmonary disease. Crit Care Med 23:1807–1815
12. Marelich GP, Murin S, Battistella F, Inciardi J, Vierra T, Roby M (2000) Protocol weaning of mechanical ventilation in medical and surgical patients by respiratory care practitioners and nurses: effect on weaning time and incidence of ventilator-associated pneumonia. Chest 118:459–467
13. Zack JE, Garrison T, Trovillion E, Clinkscale D, Coopersmith CM, Fraser VJ, Kollef MH (2002) Effect of an education program aimed at reducing the occurrence of ventilator-associated pneumonia. Crit Care Med 30:2407–2412
14. Babcock HM, Zack JE, Garrison T, Trovillion E, Jones M, Fraser VJ, Kollef MH (2004) An educational intervention to reduce ventilator-associated pneumonia in an integrated health system .A comparison of effects. Chest 125:2224–2231
15. Craven DE (2006) Preventing ventilator-associated pneumonia in adults: sowing seeds of change. Chest 130:251–260
16. Ramirez P, Ferrer M, Torres A (2007) Prevention measures for ventilator-associated pneumonia: a new focus on the endotracheal tube. Curr Opin Infect Dis 20:190–197
17. Berra L, Curto F, Bassi GL, Laquerriere P, Pitts B, Baccarelli A, Kolobow T (2008) Antimicrobial-coated endotracheal tubes: an experimental study. Intensive Care Med DOI 10.1007/s00134-008-1099-3
18. Berra L, Kolobow T, Laquerriere P, Pitts B, Bramati S, Pohlmann J, Marelli C, Panzeri M, Brambillasca P, Villa F, Baccarelli A, Bouthors S, Stelfox HT, Bigatello LM, Moss J, Pesenti A (2008) Prevention of bacterial colonization by use of endotracheal tubes internally coated with silver sulfadiazine in polyurethane: a clinical trial. Intensive Care Med DOI 10.1007/s00134-008-1100-1
19. Ahearn DG, Grace DT, Jennings MJ, Borazjani RN, Boles KJ, Rose LJ, Simmons RB, Ahanotu EN (2000) Effects of hydrogel/silver coatings on in vitro adhesion to catheters of bacteria associated with urinary tract infections. Curr Microbiol 41:120–125
20. Gabriel MM, Sawant AD, Simmons RB, Ahearn DG (1995) Effects of silver on adherence of bacteria to urinary catheters: in vitro studies. Curr Microbiol 30:17–22
21. Berra L, De Marchi L, Yu ZX, Laquerriere P, Baccarelli A, Kolobow T (2004) Endotracheal tubes coated with antiseptics decrease bacterial colonization of the ventilator circuits, lungs, and endotracheal tube. Anesthesiology 100:1446–1456
22. Saint S, Elmore JG, Sullivan SD, Emerson SS, Koepsell TD (1998) The efficacy of silver-coated urinary catheters in preventing urinary tract infection: A meta-analysis. Am J Med 105:236–241
23. Olson ME, Harmon BG, Kollef MH (2002) Silver-coated endotracheal tubes associated with reduced bacterial burden in the lungs of mechanically ventilated dogs. Chest 121:863–870
24. Berra L, De Marchi L, Yu ZX, Laquerriere P, Baccarelli A, Kolobow T (2004) Endotracheal tubes coated with antiseptics decrease bacterial colonization of the ventilator circuits, lungs and endotracheal tube. Anesthesiology 100:1446–1456
25. Rello J, Kollef MH, Diaz E, Sandiumenge A, del Castillo Y, Corbella X, Zachskorn R (2006) Reduced burden of bacterial airway colonization with a novel silver-coated endotracheal tube in a randomized multiple-center feasibility study. Crit Care Med 34:2766–2772
26. Kollef MH, Afessa B, Anzueto A, Schinner R (2007) Randomized study of a silver-coated endotracheal tube to reduce the incidence of ventilator-associated pneumonia. Intensive Care Med [Suppl September]:S65
27. Masterton R, Crave D, Rello J, Struelens M, Frimodt-Moller N, Chastre J, Ortqvist A, Cornaglia G, Lode H, Giamarellou H, Bonten MJ, Eraksoy H, Davey P (2007) Hospital-acquired pneumonia guidelines in Europe: a review of their status and future development. J Antimicrob Chemother 60:206–213
28. Resar R, Pronovost P, Haraden C, Simmnonds T, Rainey T, Nolan T (2005) Using a bundle approach to improve ventilator care processes and reduce ventilator-associated pneumonia. Jt Comm J Qual Patient Saf 31:243–248
29. Pronovost P, Needham D, Berenholtz S, Sinopoli D, Chu H, Cosgrove S, Sexton B, Hyzy R, Welsh R, Roth G, Bander J, Kepros J, Goeschel C (2006) An intervention to decrease catheter-related bloodstream infections in the ICU. N Engl J Med 355:2725–2732