Application of ventilator care bundle and its impact on ventilator associated pneumonia incidence rate in the adult intensive care unit

Syed Z. Bukhari, MPhil, PhD, *Waleed M. Hussain,* KFUF, ARIM, *Abdulhakeem A. Banjar,* MBBS, DCH, *Mohammad I. Fatani,* MD, KFUF, *Talal M. Karima,* MD, KFUF, *Ahmad M. Ashshi,* MSc, PhD.

ABSTRACT

الأهداف: الحد من معدل الإصابة بالالتهاب الرئوي الناتج عن التنفس الاصطناعي، والتقليل من تكلفة الرعاية الصحية، بالإضافة إلى ربط معدل الامتثال بحزمة الوقاية من التنفس الاصطناعي مع معدل الإصابة بهذا المرض.

الطريقة: أُجريت هذه الدراسة الاستطلاعية الطولية في قسم العناية المركزة للكبار، مستشفى حراء العام، مكة المكرمة، المملكة العربية السعودية خلال الفترة من يناير إلى ديسمبر 2010م. لقد قمنا بتطبيق معايير المستشفى والخاصة بحزمة الوقاية من الالتهاب الرئوي الناتج عن التنفس الاصطناعي وهي كالتالي: ارتفاع زاوية رأس السرير، وإعطاء المريض راحة من التخدير يومياً جنباً إلى جنب مع تقييم استعداد المريض تجاه إيقاف التنفس الصناعي، والوقاية من مرض القرحة الهضمية، والوقاية من تخثر الأوردة العميقة.

النتائج: شملت الدراسة 2747 مريض، وقد كان معدل الامتثال بحزمة الوقاية من الالتهاب الرئوي الناتج عن التنفس الاصطناعي في يناير 2010م 30%، ووصلت إلى 100% في ديسمبر 2010، في حين كان المعدل العام 78.9%. لقد كان معدل الامتثال بالحزمة الفردية على النحو التالي: ارتفاع زاوية رأس السرير (99.9%)، والراحة اليومية من التخدير (88.9%)، والوقاية من القرحة الهضمية (94.98%)، والوقاية من تخثر الأوردة العميقة (85.7%). في البداية كان معدل الالتهاب الرئوي الناتج عن التنفس الاصطناعي إلى أيام التنفس الصناعي 2.5 لكل 1000 يوم، وانخفضت إلى 0.54 في الشهر التالي. وكان المعدل الإجمالي للمرض في عام 2010 1.98 مع انخفاض إلى 1.41 لكل 1000 يوم مقارنة مع نفس البيانات التي تم جمعها في عام 2009م بأثر رجعي. وانخفضت التكلفة الإجمالية في عام واحد 154930 دولار أمريكي. ولقد تم العثور على علاقة ذات دلالة إحصائية بين معدل الالتهاب الرئوي الناتج عن التنفس الاصطناعي ومدى الامتثال بحزمة الوقاية من المرض (p=0.001). كما تم العثور على مسببات الأمراض الأكثر شيوعاً وهي كالتالي: الزائفة الزنجارية 30.7% من كل العزلات، تلتها الجرثومة الراكدة 27.7%، ثم المكورات العنقودية الذهبية 15.4%

خاتمة: أثبتت الدراسة بأن تطبيق حزمة الوقاية من الالتهاب الرئوي الناتج عن التنفس الاصطناعي قد أدى إلى انخفاض معدل الإصابة بهذا المرض، وكان هذا التحسن مستمراً وفعالاً من حيث التكلفة.

Objectives: To reduce ventilator associated pneumonia (VAP) incidence rate, lessen the cost of care, and correlate VAP bundles compliance with VAP incidence rate.

Methods: This study was a prospective longitudinal study conducted on adult intensive care unit (ICU) patients at Hera General Hospital, Makkah, Kingdom of Saudi Arabia from January to December 2010. The following Institute for Healthcare Improvement VAP prevention bundle was applied: head-of-bed elevation; daily "sedation-vacation" along with a readiness-to-wean assessment; peptic ulcer disease (PUD) prophylaxis; and deep venous thrombosis (DVT) prophylaxis.

Results: Among a total of 2747 patients, the bundle compliance rate in January 2010 was 30%, and reached to 100% in December 2010, while the overall rate was 78.9%. The individual bundle compliance rates were as follows: head-of-bed elevation - 99.9%; daily sedation vacation - 88.9%; PUD prophylaxis - 94.9%; and DVT prophylaxis - 85.7%. At the beginning, VAP rate was 2.5/1000 ventilator days, and reduced to 0.54 in the next month. The overall VAP incidence rate in 2010 was found to be 1.98 with a reduction of 1.41 by comparing with the same data of year 2009 collected retrospectively. The total reduction cost in one year was $154,930. A significant correlation was found between the VAP rate and its bundle compliance (p=0.001). Most frequent pathogens found were *Pseudomonas aeruginosa* (30.8% of all isolates) followed by *Acinetobacter baumannii* (27.7%), and methicillin-resistant *Staphylococcus aureus* (15.4%).

Conclusion: Application of VAP prevention bundle reduced the VAP incidence rate and lowered the cost of care.

Saudi Med J 2012; Vol. 33 (3): 278-283

From the Departments of Infection Prevention and Control (Bukhari), Department of Internal Medicine (Hussain, Karima), Pediatrics (Banjar), Dermatology (Fatani), Hera General Hospital, and Department of Laboratory Medicine (Ashsni), Faculty of Applied Medical Sciences, Umm Al-Qura University, Makkah, Kingdom of Saudi Arabia.

Received 30th November 2011. Accepted 8th February 2012.

Address correspondence and reprint request to: Dr. Syed Z. Bukhari, Department of Infection Prevention and Control, Hera General Hospital, PO Box 20865, Makkah, Kingdom of Saudi Arabia. Tel. +966 (2) 5203535. Fax. +966 (2) 5200333. Email: zahidbukhari100@msn.com

Surveillance of healthcare-associated infections (HAI) is an integral part of infection prevention and control programs of a hospital, especially in the intensive care unit (ICU) setting. Bundles have found their greatest application in the prevention of HAI, which are a major cause of morbidity and mortality in intensive care patients.[1,2] A bundle is defined as a small, straightforward set of scientifically grounded elements that when implemented together, result in better outcomes than when implemented individually.[3] Bundles have found their greatest application in the prevention of HAIs. The device associated HAI specifically, ventilator associated pneumonia (VAP) is known to increase the duration of mechanical ventilation, length of stay, and also cost of care.[4,5] Initiation of a VAP bundle protocol is an effective method for VAP reduction when compliance is maintained.[6] The current study was aimed to find out the incidence rate of VAP and its association with compliance rate of VAP bundle in adult ICU, to determine the sustainability over a one year period, and to estimate the cost of care for VAP infections by comparing incidence rates before the application of bundles. Understanding the incremental cost-effectiveness of VAP bundles can help prioritize efforts to minimize the associated morbidity.[7]

Methods. This is a prospective longitudinal study conducted at the adult medical and surgical intensive care unit (MSICU) at Hera General Hospital (HGH), Makkah, Kingdom of Saudi Arabia. The HGH is a secondary care unit with 280 bed capacity including 18 beds MSICU. This study has been approved by the ethical committee of the hospital, and followed the principles of Helsinki Declaration. The VAP bundle program began in January 2010, and the compliance data were collected from then until December 2010, for a one year period. All patients on mechanical ventilator were selected and assessed for compliance with the all key elements of VAP Prevention Bundle in ICU, while non-ventilated patients in ICU were excluded from the study. The VAP was defined as pneumonia when patient was intubated and ventilated at the time of, or within 48 hours before the onset of the event. There is no minimum period of time that the ventilator must be in place in order for pneumonia to be considered ventilator-associated.[7] Clinically supported by the evidence that he or she developed a new fever and cough with development of purulent sputum, in combination with radiological evidence of a new or progressive pulmonary infiltrate, leukocytosis, a suggestive gram stain, and growth of bacteria in cultures of sputum, tracheal aspirate, pleural fluid, or blood.[8] There was no minimum period of time that the ventilator must be in place in order for pneumonia to be considered ventilator-associated. The VAP rate was defined as the number of ventilator-associated pneumonias per 1,000 ventilator days as per Centre for Disease Control and Prevention (CDC) definition.[9] A day on mechanical ventilation was defined as a patient who was on mechanical ventilator at 12 midnight. Weaning was defined as the first day where the patient was either extubated without non-invasive ventilation, or in case of patients with a tracheostomy, able to breathe spontaneously without mechanical support. Standard precautions were applied to all patients, including hand washing before dealing with the patient's daily oral care[10] and sterile tracheal suction with closed-system. An active surveillance protocol was applied in the MSICU based on the recent CDC guideline.[8] The ventilator bundle protocol of 4 elements from the Institute for Healthcare Improvement (IHI)[11] was applied. If even a single missing element of bundles was either not carried out, or are not documented, the whole bundle was considered not applied. The compliance was measured with the entire ventilator bundle, not just parts of it. When the bundle element was contraindicated for a particular patient, and it was documented appropriately in the medical record, then the patient was considered compliant with regard to that measure. The protocol of VAP bundle application followed is provided as follows: the head of the patient's bed was elevated between 30 and 45 degrees to reduce aspiration pneumonia, to improve ventilation, and to make the patient comfortable.[12] To fulfill the compliance, the following actions were taken: check list on nursing flow sheets was given and each topic was discussed at multidisciplinary rounds; respiratory therapists worked collaboratively with nurses; visitors and family education was given and explained to them that if the bed is not at required position, immediately inform the treating nurse; initiation and weaning of mechanical ventilation was carried out by delivery of tube feedings with provision of oral care.[13] The elevation of bed was encouraged and the ICU staff was motivated. The protocol for daily sedation vacation and daily assessment of readiness to extubate was applied for the following reasons; to promote weaning, to increase potential for self-extubation, to reduce pain and anxiety, and to promote early extubation. The lighter sedation protocol was followed by daily assessment for neurological readiness to extubate. The patient care team increased monitoring and vigilance to prevent self-extubation. The weaning protocol was followed by preparing a plan to wean the patient from the ventilator, and added to the "sedation vacation" component of the

bundle. The Riker Sedation Agitation Scale (SAS)[14] was followed and implemented to avoid over sedation. The compliance assessment was carried out every day on multidisciplinary rounds. Deep venous thrombosis (DVT) prophylaxis was applied to prevent venous thromboembolism, or other complications based on solid evidence.[15] Upon admission, DVT prophylaxis was included on the VAP bundle order sheet. The treating physician prescribed the appropriate medication in the medical record, and the administration of the medication was signed by the nurse. It was discussed daily during multidisciplinary rounds. Peptic ulcer disease (PUD) prophylaxis was applied to reduce acid production in the stomach, and consequent risk of bleeding from gastric erosions and peptic ulcers. Two pH-altering drugs were used according to treating physician order; H2 receptor inhibitors and proton pump inhibitor-esomeprazole per oral (PO) was given if the patient was on nasogastric tube, or alternatively pantoprazole (IV+ PO) was implied. The requirement for PUD prophylaxis remains, since it serves to underscore excellent ventilator care and raise awareness surrounding best ventilator practices.[16] The study proposal was approved 2 months prior to implementation. The scientific background, technique of the bundle along with its compliance monitoring and documentation were taught to all concerned nurses and residents of the ICU in weekly seminars by the heads of ICU and Infection Prevention and Control. Two surveys entitled knowledge, attitude and practice (KAP) of ICU staff on VAP bundles were conducted in teaching sessions. The VAP incidence rate of year 2010 after application of bundles was compared with VAP incidence rate of one year period (2009) when the VAP bundles were not applied. The VAP data of 2009 was collected by record review of surveillance of HAI conducted by the Infection Prevention and Control Department. The VAP incidence rate during the study period was compared with international benchmarks-National Healthcare Safety Network (NHSN) data.[17] The primary endpoint of the study was adherence to the ventilator bundle. Secondary endpoints were: rate of pneumonia; days on mechanical ventilation; and length of stay on the ICU.

A $p<0.05$ was considered statistically significant. The 95% confidence interval between upper and lower limit was selected. Data were analyzed with Statistical Package for Social Sciences 10.0 version (SPSS Inc., Chicago, IL, USA).

Results. During January to December 2010, there were 2747 patients who were on mechanical ventilator in ICU, and the overall VAP incidence rate was 1.98 infections per 1,000 patient's days. The overall VAP compliance rate of 4 elements of the bundles was found to be 78.9%. The incidence rate of VAP and overall compliance rate of ventilator bundle is shown in **Figure 1**. A significant correlation was found between the VAP rate and its bundle compliance (p=0.001). The overall compliance with the 4 bundle elements by January was 30%, and reached to 100% in December. The individual bundles compliance rate was found as follows: head-of-bed elevation (99.8%); daily sedation vacation (88.9%); PUD prophylaxis (94.9%), and DVT prophylaxis (85.7%). **Figure 2** illustrates the compliance rate of 4 key elements individually, and also shows that there was a sustainable improvement in compliance rates in the second half period of the study. On first evaluation of KAP survey, the ICU staff showed full awareness regarding bundles (fully met) was 14.2%, awareness regarding few complements (partially met) was 42.8%, and did not know anything (not met) was 35.7%. The second KAP evaluation result was as follows: fully met (50%); partially met (35%); and not met (15%). At the start of the project, VAP rate was 2.5 per 1,000 ventilator days. While the progressive implementation of the bundle elements and extensive education brought a rapid decline of incidence rates, the significant reduction in rates was noted in the second month. The overall VAP rate in 2009 was 3.39, and in 2010 was found to be 1.98 per 1000 ventilator days. The reduction of VAP rate in 2010 was 1.41 infections per 1000 ventilator days. **Figure 3** shows the correlation of incidence rate of ventilator associated pneumonia with the NHSN benchmarks. The most frequent pathogens isolated were: *Pseudomonas aeruginosa (P. aeruginosa)* (30.8%) of all isolates; *Acinetobacter baumannii (A. baumannii)* (27.7%); methicillin resistant *Staphylococcus aureus* (MRSA) (15.4%); *Klebsiella pneumonia* (*K. pneumonia)* (13.8%), *Escherichia coli* (7.7%), and *Staphylococcus aureus* (1.5%). All *A. baumannii* isolates were resistant to all antibiotics tested including carbapenem - pan resistant while other 2 frequent gram negative organisms were found multi-drug resistant (MDR) *P. aeruginosa* (93.1%) and *K. pneumonia* (82.8%). It was estimated that each VAP case increased the hospital length of stay attributable by 10 days, and the mean hospital cost by $40,000.[18] In the current study, the incidence rate of VAP decreased to 1.41 cases/1000 ventilator days, and saving cost was $56,400/1000 ventilator days. The number of ventilator days was 2447, therefore the total saving cost in one year was $154,930.

Discussion. The ventilator bundle was designed as part of an overall strategy to improve the care of ventilated

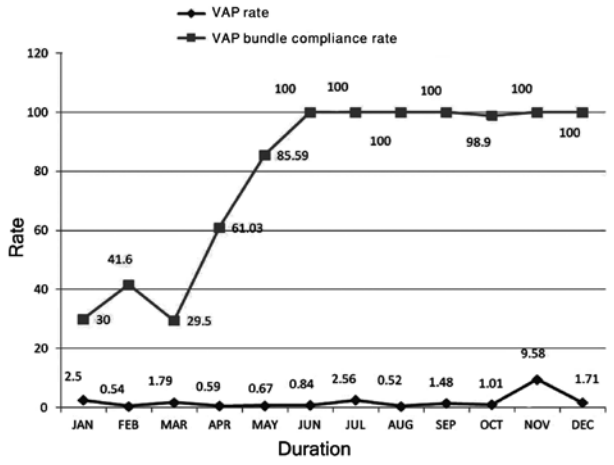

Figure 1 - Correlation of incidence rate ventilator associated pneumonia (VAP) and overall VAP bundle compliance rate.

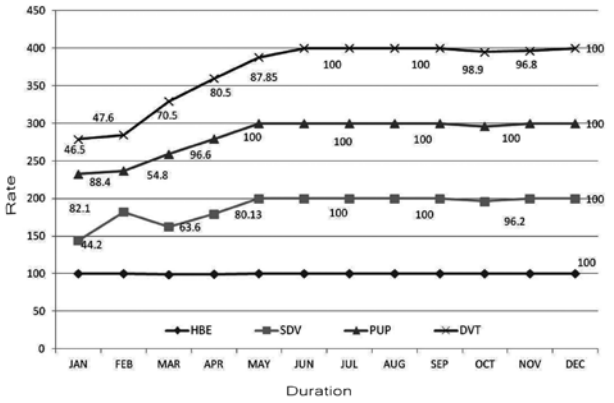

Figure 2 - Individual compliance rate of the 4 key components of ventilator associated pneumonia bundle.

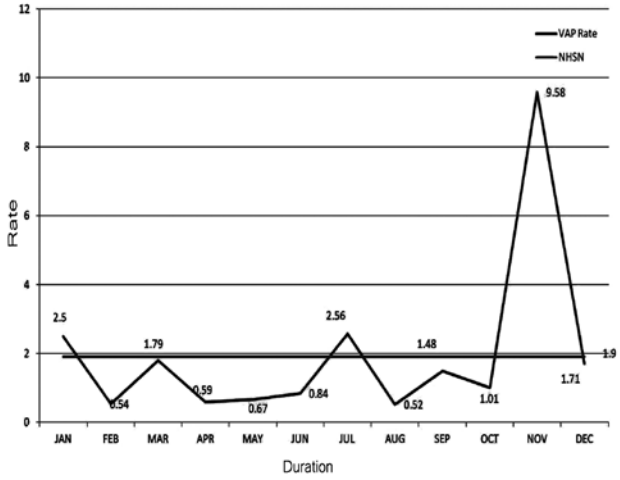

Figure 3 - Correlation of incidence rate of ventilator associated pneumonia (VAP) with and National Healthcare Safety Network (NHSN)[30] (p=0.001)

patients.[11] The original intent was to reduce VAP rates, as well as to provide best care for patients on ventilators. The current study showed that VAP prevention bundle management of patients on mechanical ventilators in ICU decreased the risk of VAP, and improved the outcome of patients. Although the staff was trained on bundle compliance prior to the study, however still at the start of the project, VAP incidence rate was 2.4 per 1,000 ventilator days. The progressive implementation of the various bundle elements brought a rapid decline in VAP rate. The substantial reduction in rates was noted on the second month of the study. The team celebrated the success when data of the second month was presented, showing a rapid drop of VAP incidence rate and tremendous improvement in bundle compliance. After a 6 months period, the compliance rate reached to 100%, and it continued to remain the same up to the end of the study, and this is similar to the results found in another study[12] showing a sustainable improvement using the quality audit tool. The VAP incidence rate of the current study was found at a lesser level than Gikas et al[4] and Hawe et al,[19] while remained higher than the results reported by Walkey et al[20].

This study proved that the application of VAP prevention bundles is an evidence-based clinical practice as our compliance rate directly affects the VAP incidence rate throughout the study period similar to various other studies[21,22] except in the month of November 2010. In the same month, we also noticed that there was high VAP incidence rate by comparing NHSN bench marking. We investigated it as an outbreak of VAP in this particular period. We defined a problem as high VAP incidence rate in one particular month in spite of 100% VAP bundle compliance rate. We applied quality tools, that is, root cause analysis. On reviewing HAI surveillance data and microbiology culture, it was found that *P. aeruginosa* with the same antibiogram was the predominant organism. The following known risk factors commonly associated with high VAP rate were analyzed by reviewing the Infection Control Daily Audit sheet: distance between the ICU patients was >1.2 meters; patient nurse ratio was 1:1, hand hygiene and other infection control material like personnel protective equipment (PPE) were readily available; hand hygiene compliance rate of healthcare professional was consistent with previous months; all patients were on appropriate antibiotics according to the antimicrobial susceptibility testing reports; isolation precautions were followed when indicated; the quality control of sterilization of the ventilators were found in satisfactory condition by the available instrument tracking system; no host factors like underlying medical conditions,

immunosuppression, chronic obstructive diseases were observed among the study patients; and no problem on device factors like endotracheal tube, orogastric, or nasogastric tubes were found, except ventilator circuit. The only supportive findings noticed was that the ventilator care in this particular time was carried out by open system due to the shortage of closed system. This was the understandable reason of this variation. From surveillance point of view, identifying the VAP rates for one month in one unit/facility does not allow for enough data to make the comparison to NHSN aggregate data (the benchmark) statistically significant (p=0.001, 95% confidence interval: 0.52-9.58). We confirmed that our bundle application team was well educated regarding the bundle. Ongoing surveillance and re-education and reinforcement were also part of a strong infection prevention program.[23] Prior to initiation of the bundle, VAP was seen at a rate of 3.39 cases/1000 ventilator days in 2009 (endemic rate), while after application of bundles it was 1.98 cases/1000 ventilator days. This resulted in the reduction of VAP rates by 1.41 cases per 1000 ventilator-days. The outcome of the current study in patient care improvement was supported by various other studies.[21,24,25] The estimated reduction cost by the application of bundles was found similar to another local study[26] and international studies[25,27].

The following recommendations were endorsed for adult ICU: continue VAP prevention bundle as it proved an effective measure; monitor the VAP incidence rates with endemic rate or NHSN benchmarking; and used closed ventilator circuit. The 3 most frequent microorganisms of the current study, that is, *P. aeruginosa, A. baumannii,* and *K. pneumoniae* were also the common pathogens responsible for VAP which is similar to other studies[28,29]. The resistance among the microorganism isolated could be the contributory factors of morbidity and mortality of patients on mechanical ventilators.

In conclusion, the VAP bundle implementation in ICU dramatically reduced the VAP incidence rate and was found cost-effective. There was a significant correlation VAP incidence rate with its bundle compliance. Although there was inconsistency of VAP bundle compliance rate at the beginning but due to better outcome, its application was recommended to be continued as a routine practice in ICU, and integrate VAP prevention with other quality improvement programs of ICU. Sustained high compliance rate of VAP bundle may give more promising results in the future. The current study will be further extended to explore the reasons of non-compliance of VAP bundles.

Acknowledgment. *The authors gratefully acknowledge Dr. Khalid Hakim, Consultant, ICU, Dr. Salah Aburubu (Quality Designee, ICU), Ms. Eleanor Reinli, Supervisor, QPSA, Ms. Catalina Calixton, Ms. Faten Felemban, Ms. Liza Baylon, Ms. Sitte Rehma (Infection Prevention and Control Department), Ms. Afaf Irenea, and Ms. Fatima Hariri (Microbiology), Hera General Hospital, Makkah, Kingdom of Saudi Arabia on their support in conducting this study. Special thanks to Syed Faran Bukhari (student, London School of Economics, UK) for helping in data analysis.*

References

1. Werarak P, Kiratisin P, Thamlikitkul V. Hospital-acquired pneumonia and ventilator-associated pneumonia in adults at Siriraj Hospital: aetiology, clinical outcomes, and impact of antimicrobial resistance. ***J Med Assoc Thai*** 2010; 93 (Suppl 1): S126-S138.
2. Noor A, Hussain SF. Risk factors associated with development of ventilator associated pneumonia. ***J Coll Physicians Surg Pak*** 2005; 15: 92-95.
3. Marra AR, Cal RG, Silva CV, Caserta RA, Paes AT, Moura DF Jr, et al. Successful prevention of ventilator-associated pneumonia in an intensive care setting. ***Am J Infect Control*** 2009; 37: 619-625.
4. Gikas A, Roumbelaki M, Bagatzouni-Pieridou D, Alexandrou M, Zinieri V, Dimitriadis I, et al. Device-associated infections in the intensive care units of Cyprus: results of the first national incidence study. ***Infection*** 2010; 38: 165-171.
5. Nolan SW, Burkard JF, Clark MJ, Davidson JE, Agan DL. Effect of morbidity and mortality peer review on nurse accountability and ventilator-associated pneumonia rates. ***J Nurs Adm*** 2010; 40: 374-383.
6. Bird D, Zambuto A, O'Donnell C, Silva J, Korn C, Burke R, et al. Adherence to ventilator-associated pneumonia bundle and incidence of ventilator-associated pneumonia in the surgical intensive care unit. ***Arch Surg*** 2010; 145: 465-470.
7. Zilberberg MD, Shorr AF. Ventilator-associated pneumonia as a model for approaching cost-effectiveness and infection prevention in the ICU. ***Curr Opin Infect Dis*** 2011; 24: 385-389.
8. Singh S, Pandya Y, Patel R, Paliwal M, Wilson A, Trivedi S. Surveillance of device-associated infections at a teaching hospital in rural Gujarat--India. ***Indian J Med Microbiol*** 2010; 28: 342-347.
9. Horan TC, Andrus M, Dudeck MA. CDC/NHSN surveillance definition of healthcare-associated infection and criteria for specific types of infections in the acute care setting. ***Am J infect Control*** 2008; 36: 309-332.
10. Fields LB. Oral care intervention to reduce incidence of ventilator-associated pneumonia in the neurologic intensive care unit. ***J Neurosci Nurs*** 2008; 40: 291-298.
11. Youngquist P, Carroll M, Farber M, Macy D, Madrid P, Ronning J, et al. Implementing a ventilator bundle in a community hospital. ***Jt Comm J Qual Patient Saf*** 2007; 33: 219-225.
12. Niël-Weise BS, Gastmeier P, Kola A, Vonberg RP, Wille JC, van den Broek PJ. An evidence-based recommendation on bed head elevation for mechanically ventilated patients. ***Crit Care*** 2011; 15: R111.
13. Wip C, Napolitano L. Bundles to prevent ventilator-associated pneumonia: how valuable are they? ***Curr Opin Infect Dis*** 2009; 22: 159-166.

14. Jackson DL, Proudfoot CW, Cann KF, Walsh TS. The incidence of sub-optimal sedation in the ICU: a systematic review. ***Crit Care*** 2009; 13: R204.
15. Manoel AL, Boszczowski I, Andrade AH, Bierrenbach L, Taira E, Baruzzi AC. Successful strategy to reduce ventilator-associated pneumonia. ***Crit Care*** 2010; 14: 83.
16. Alsultan MS, Mayet AY, Malhani AA, Alshaikh MK. Pattern of Intravenous Proton Pump Inhibitors Use in ICU and Non-ICU Setting: A Prospective Observational Study. ***Saudi J Gastroenterol*** 2010; 16: 275-279.
17. Edwards JR, Peterson KD, Mu Y, Banerjee S, Allen-Bridson K, Morrell G, et al. National Healthcare Safety Network (NHSN) report: data summary for 2006 through 2008, issued December 2009. ***American Journal of Infection Control*** 2009; 37: 783-805.
18. Dubose J, Teixeira PG, Inaba K, Trankiem C, Teixeira PG, Salim A, et al. Measurable outcomes of quality improvement using a daily quality rounds checklist: one-year analysis in a trauma intensive care unit with sustained ventilator-associated pneumonia reduction. ***J Trauma*** 2010; 69: 855-860.
19. Hawe CS, Ellis KS, Cairns CJ, Longmate A. Reduction of ventilator-associated pneumonia: active versus passive guideline implementation. ***Intensive Care Med*** 2009; 35: 1180-1186.
20. Walkey AJ, Reardon CC, Sulis CA, Nace RN, Joyce-Brady M. Epidemiology of ventilator-associated pneumonia in a long-term acute care hospital. ***Infect Control Hosp Epidemiol*** 2009; 30: 319-3124.
21. Albertos R, Caralt B, Rello J. Ventilator-associated pneumonia management in critical illness. ***Curr Opin Gastroenterol*** 2011; 27: 160-166.
22. Resar R, Pronovost P, Haraden C, Simmonds T, Rainey T, Nolan T. Using a bundle approach to improve ventilator care processes and reduce ventilator-associated pneumonia. ***Jt Comm J Qual Patient Saf*** 2005; 31: 243-248.
23. Aragon D, Sole ML. Implementing best practice strategies to prevent infection in the ICU. ***Crit Care Nurs Clin North Am*** 2006; 18: 441-452.
24. Bloos F, Müller S, Harz A, Gugel M, Geil D, Egerland K, et al. Effects of staff training on the care of mechanically ventilated patients: a prospective cohort study. ***Br J Anaesth*** 2009; 103: 232-723.
25. Bird D, Zambuto A, O'Donnell C, Silva J, Korn C, Burke R, et al. Adherence to ventilator-associated pneumonia bundle and incidence of ventilator-associated pneumonia in the surgical intensive care unit. ***Arch Surg*** 2010; 145: 465-470.
26. Al-Tawfiq JA, Abed MS. Decreasing ventilator-associated pneumonia in adult intensive care units using the Institute for Healthcare Improvement bundle. ***Am J Infect Control*** 2010; 38: 552-556.
27. Cocanour CS, Peninger M, Domonoske BD, Li T, Wright B, Valdivia A, et al. Decreasing ventilator-associated pneumonia in a trauma ICU. ***J Trauma*** 2006; 61: 122-130.
28. Nseir S, Ader F, Lubret R, Marquette CH. Pathophysiology of Airway Colonization in Critically Ill COPD Patient. ***Curr Drug Targets*** 2011; 12: 514-520.
29. Cai XD, Cao Y, Chen C, Yang Y, Wang CQ, Zhang L, et al. Investigation of nosocomial infection in the neonatal intensive care unit. ***Zhongguo Dang Dai Er Ke Za Zhi*** 2010; 12: 81-84.
30. Centres for Disease Control and Prevention. CDC/NHSN surveillance definition of health care-associate infection and criteria for specific types of infections in the acute care setting. ***Am J Infect Control*** 2008; 36: 309-332.

Illustrations, Figures, Photographs

Four copies of all figures or photographs should be included with the submitted manuscript. Figures submitted electronically should be in JPEG or TIFF format with a 300 dpi minimum resolution and in grayscale or CMYK (not RGB). Printed submissions should be on high-contrast glossy paper, and must be unmounted and untrimmed, with a preferred size between 4 x 5 inches and 5 x 7 inches (10 x 13 cm and 13 x 18 cm). The figure number, name of first author and an arrow indicating "top" should be typed on a gummed label and affixed to the back of each illustration. If arrows are used these should appear in a different color to the background color. Titles and detailed explanations belong in the legends, which should be submitted on a separate sheet, and not on the illustrations themselves. Written informed consent for publication must accompany any photograph in which the subject can be identified. Written copyright permission, from the publishers, must accompany any illustration that has been previously published. Photographs will be accepted at the discretion of the Editorial Board.