DEVICE-RELATED INFECTIONS IN CRITICALLY ILL PATIENTS. PART II: PREVENTION OF VENTILATOR-ASSOCIATED PNEUMONIA AND URINARY

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REVIEW

Device-Related Infections in Critically Ill Patients. Part II: Prevention of Ventilator-Associated Pneumonia and Urinary Tract Infections

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Summary

Device utilization in critically ill patients is responsible for a high risk of complications such as catheter-related bloodstream infections (CRBSI), ventilator-associated pneumonia (VAP) and urinary tract infections (UTI). In this article we will review the current status of data regarding the prevention of VAP and UTI. The results of the more recent (5 years) randomized controlled trials are reviewed and discussed. General recommendations include staff education and use of a surveillance program with a restrictive antibiotic policy. Adequate time must be allowed for hand washing and barrier precautions must always be used during device manipulation.

Specific measures for VAP prevention are: 1) use of multi-use, closed-system suction catheters; 2) no routine change of the breathing circuit; 3) lubrication of the cuff of the endotracheal tube (ET) with a water-soluble gel; 4) maintenance of patient in semi-recumbent position to improve chest physiotherapy in intubated patients.

Specific measures for UTI prevention include: 1) use of a catheter-valve instead of a standard drainage system; 2) use of a silver-alloy, hydro gel-coated latex urinary catheter instead of uncoated catheters.

Biofilm represents a new variable: the capacity of bacteria to organize a biofilm on a device surface can explain the difficulty in preventing and eradicating an infection in a critically ill patient.

More clinical trials are needed to verify the efficacy of prevention measures of ICU infections.

Key words: **Critically ill patients, nosocomial infection, Intensive Care Unit, biofilm, device, catheters, pneumonia.**

VENTILATOR-ASSOCIATED PNEUMONIA (VAP) PREVENTION

Ventilator-associated pneumonia (VAP) refers to nosocomial pneumonia which has developed more than 48 hours after tracheal intubation and mechanical ventilation. VAP is associated with an approximately 4-day increase in length of Intensive Care Unit (ICU) stay and an attributed mortality of approximately 20-30% [1].

Fixed VAP risk factors include underlying cardiorespiratory disease, neurological injury and trauma. Modifiable VAP risk factors include some aspects of general ICU management and ventilator and airway management (*Table 1*) [1].

There is a great deal of controversy about methods for preventing this infection. Prevention of VAP relies on basic infection control practices and on many specific strategies for interfering with colonization routes (for example the selective decontamination of the digestive tract).

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TABLE 1 - *Risk factors for VAP (from 1).*

Related to:	
Population	Age
	Cardio-respiratory disease
	COPD
	Adult respiratory distress syndrome (ARDS)
	Coma
	Neurosurgery
	Head trauma, polytrauma
	Burns
	Organ Failure (OSF)
Ventilator and airway management	Mechanical Ventilation
	Intracuff pressure <20 cm H_2O
	Reintubation
	24-hour circuit changes
	Tracheostomy
	Failed subglottal aspiration
General ICU management	Enteric nutrition
	Supine positioning
	Aspiration
	H2-receptor antagonists
	Paralytic agents
	Antibiotics
	Transport out of the ICU

General recommendations

Infection control for VAP should be based on staff education and infection surveillance programs. It seems to be useful to educate healthcare workers regarding risks of bacterial pneumonia and the procedures that patients need. In one recent trial, an educational program conducted on 16 intensive care nurses improved their practice of tracheal suctioning, thus minimizing the risk of infection transmission; as a result they showed significant improvements in both knowledge and practice of the maneuver [2].

A surveillance program for bacterial pneumonia in ICU patients at high risk for nosocomial pneumonia to determine trends and identify potential problems, including data regarding the causative microorganisms and their antimicrobial susceptibility patterns, is also useful. Data should be presented as rates (e.g. number of infected patients or infections per 100 ICU days or per 1,000 ventilator-days) to facilitate intra-hospital comparisons [3,4].

In order to avoid person-to-person transmission of bacteria, general recommendations regarding hand washing and hand rubbing [5], barrier precautions and the suction of respiratory tract secretions should be followed. Regarding this last aspect, the use of a multi-use, closed-system, suction catheter instead of the single-use, open system catheter for prevention of pneumonia seems to reduce the incidence rate of VAP without demonstrating any adverse effects [6]. In this prospective study 104 consecutive patients needing mechanical ventilation were randomized to have a closed endotracheal suctioning instead of a standard open suctioning. The results showed that the open suctioning system was accompanied by a 3.5-fold higher risk of VAP (p=0.05; 95% confidence limits = 1-12.33). The number of VAP was 9 in the open suctioning group vs 4 in the closed suctioning group. No adverse effects were observed. The authors concluded that a closed suctioning system reduces the incidence of VAP.

Management of respiratory devices

Sterilization and/or disinfection and changes of circuit component: To avoid the transmission of microorganisms, equipment and devices should be sterilized, disinfected and maintained according to the following procedures: a) sterilize or use high-level disinfection for semi-critical equipment or devices, for example, items that come into direct or indirect contact with the lower respiratory tract; b) do not routinely sterilize or disinfect the internal machinery of mechanical ventilators and do not routinely change the breathing circuit (including tubing and exhalation valve).

Regarding routine changes of circuit components Kollef *et al.* [7], in a randomized controlled trial on 300 patients, of which 147 were assigned to receive no routine circuit ventilator changes and 153 were assigned to receive circuit changes every 7 days, failed to demonstrate differences between the two groups in terms of incidence of VAP (relative risk = 0.85; 95% confidence limits = 0.55-1.17). The authors report that non-routine ventilator circuit changes can reduce medical care costs without increasing the incidence of nosocomial pneumonia in patients who require prolonged mechanical ventilation [7].

At the moment there are no recommendations regarding how often a humidifier of a ventilator in use on a patient should be changed.

It is necessary to sterilize reusable breathing circuits and bubbling, or subject them to high-level disinfection between their uses on different patients.

Periodically drain and discard any condensation that collects in the tubing of a mechanical ventilator, taking precautions not to allow condensation to drain towards the patient [8]. Wash hands after performing the procedure or handling the fluid.

It does not seem necessary to place a filter at the distal end of the expiratory-phase tubing of the breathing circuit to collect condensation.

Do not place bacterial filters between the humidifier reservoir and the inspiratory-phase tubing of the breathing circuit of a mechanical ventilator. Always use sterile water to fill the humidifier [8].

Hygroscopic condenser/humidifier or a heat-moisture exchanger: The use of a hygroscopic condenser-humidifier or a heat-moisture exchanger rather than a heated humidifier is an unresolved

issue. In 1997, Rathgeber *et al* [9] demonstrated that a heat and moisture exchanger (HME) with filters prevents contamination of the anesthesia breathing system during low flow anesthesia.

In the same year, another prospective, randomized, blinded trial on 116 patients in ICU, undergoing mechanical ventilation for a minimum of 48 hours, showed that circuits with a bacterial-viral filtering heat and moisture exchanger are less readily colonized by bacteria but failed to demonstrate VAP prevention [10].

Patients were randomized to three ventilation groups using: a) a hot water humidifier circuit with a 2-day circuit change (n = 41); or b) a bacterial-viral filtering HME in the circuit, with either a 2-day (n = 42); or c) a 4-day circuit change (n = 33). Sixty-seven percent of hot water circuits became contaminated compared with 12% in the two HME groups (p <0.0001). Median colony counts were lower in the HME groups (p <0.0001). But the frequency of VAP and the volume and fluidity of secretions were similar for all groups [10].

In a study conducted on 243 consecutive critically ill adult patients who required mechanical ventilation for 48 hours or more, the VAP rate of the group with HME was 11.4% and that for the group with a heated humidifying system was 15.8% (the difference was not statistically significant). Therefore, the results regarding bacterial colonization of respiratory devices were different: approximately 68% of the patients in the HME group had no pathogen isolated compared with 50% of the patients in the heated humidifying system group: this difference was statistically significant (P≤0.01). The authors conclude that even though the study did not find HME to be significantly advantageous in VAP prevention, other advantages such as reduced nurse workload, reduced financial cost, and better safety make HME a more favorable device for humidification in the adult ICU [11].

However, a prospective randomized trial on 280 consecutive intubated trauma patients in a 20-bed trauma ICU randomized to either an in-line HME filter or a humidifier in the breathing circuit showed that the HME nosocomial VAP rate was 6% compared to 16% for the humidifier group (p<0.05). The lower rate was associated with a significant reduction in total ICU stay. Disposable ventilator circuit costs in the HME group were reduced compared to the humidifier group in whom circuit changes occurred at 7-day intervals [12].

More randomized studies are required to define guidelines about the use of HME in respect to the heated humidifiers. Also, their effectiveness in the prevention of VAP requires further study.

In regard to the effectiveness of HME during patient ventilation, there are few data available about when to change the hygroscopic condenser-humidifier or heat-moisture exchanger. In a prospective, controlled, randomized study on 220 consecutive, critically ill, surgical patients requiring mechanical ventilation for >48 h, it was demonstrated that changing the hydrophobic or hygroscopic HME after 3 days does not diminish efficiency, increase bacterial resistance or alter bacterial colonization. The frequency rate of nosocomial pneumonia was also unchanged (20:1000 ventilation days vs 16.6:1000 respectively). In light of these results the use of HMEs for >24 h up to 72 h, appears to be safe and cost effective [13].

Orotracheal tube: VAP prevention can be obtained by lubricating the cuff with a water-soluble gel, which might prevent aspiration by plugging the channels on the cuff wall. In a prospective study on 50 intubated patients, cuff lubrication with a water-soluble gel reduces pulmonary aspiration in anesthetized patients: lubricated cuffs were compared with unlubricated cuffs using dye leakage from the subglottal space to the tracheobronchial tree. Dye was detected clinically by dye coloration of secretions during tracheal suctioning. Dye leakage in anesthetized patients was 11% in the lubrication group and 83% in the non-lubrication group (P <0.0001) [14]. But the effectiveness of this method to prevent VAP requires clinical demonstration.

Another strategy for the prevention of VAP involves continuous subglottal suctioning. Its effectiveness was shown in 1995 on 153 patients who had been divided into 2 groups: 76 patients were randomly allocated to receive continuous aspiration of subglottal secretions, and 77 control patients were allocated to receive the usual care. The incidence of VAP was 19.9 episodes/1000 ventilator days in the patients receiving continuous aspiration of subglottal secretions and 39.6 episodes/1000 ventilator days in the control patients (relative risk, 1.98; 95% CI, 1.03 to 3.82) [15].

Recently Shorr and O'Malley, in a cost/efficacy analysis of VAP, compared the costs of continuous subglottal aspiration and standard orotracheal intubation in a hypothetical cohort of 100 patients requiring orotracheal intubation, and found that continuous subglottal suctioning may result in savings [16].

On the basis of these results the aspiration of subglottal secretions appears to be effective and efficient in the prevention of VAP and VAP-related costs. A large, prospective, multicenter study to confirm this hypothesis is desirable.

The lesson learned from this study may be that before deflating the cuff of an endotracheal tube in preparation for tube removal, it is necessary to ensure that secretions are cleared from above the tube cuff.

Tracheostomy

Percutaneous dilatational tracheostomy techniques performed with the Ciaglia Introducer Set are effective, safe and superior to conventional surgical tracheostomy. In a randomized study on 60 ICU

patients, infections complicating tracheostomy performed with the Ciaglia method vs. surgical tracheostomy were evaluated: sixty patients selected for elective tracheostomy were randomized for either Ciaglia (30 patients) or surgical tracheostomy (30 patients). Minor infections (cellulites in a few millimeters around the stoma without purulent secretion) were encountered in 3 cases in the Ciaglia group as opposed to 11 cases in the surgical tracheostomy group (P<0.01). Major infection (cellulites in several millimetres around the stoma with purulent secretions) was encountered in none versus 8 cases, respectively (P<0.01) [17]. Ciaglia methods in this small study appear to prevent major and minor local infections but the role of tracheostomy in prevention of VAP requires further research.

Patient position and physiotherapy

The semi-recumbent body position reduces frequency and risk of nosocomial pneumonia in intubated patients. This result was demonstrated in 86 intubated and mechanically-ventilated patients of one medical and one respiratory ICU at a tertiary-care university hospital. The frequency of clinically suspected nosocomial pneumonia was lower in the semi-recumbent group than in the supine group (three of 39 [8%] vs. 16 of 47 [34%]; 95% CI for difference 10.0-42.0, p=0.003). This was also true for microbiologically confirmed pneumonia (semi-recumbent: 2 of 39 [5%] vs. supine 11 of 47 [23%]; CI: 4.2-31.8, p=0.018) [18].

Furthermore, to demonstrate that chest physiotherapy designed to enhance sputum clearance could decrease the occurrence of VAP, a prospective controlled trial was performed in a tertiary teaching hospital ICU. Sixty adult patients intubated and mechanically ventilated for at least 48 h were divided into two groups: chest physiotherapy (intervention group) or sham physiotherapy (control group). VAP occurred in 39% (14/36) of the control group and in 8% (2/24) of the intervention group (OR = 0.14, 95% CI 0.03 to 0.56, P=0.02) [19]. In this small trial, chest physiotherapy in ventilated patients was independently associated with a reduction in VAP. This suggested benefit of physiotherapy in prevention of VAP requires confirmation with a larger randomized controlled trial.

Bronchoscope management

Recently a large outbreak (a total of 48 respiratory tract and bloodstream infections in 39 out of 414 patients undergoing diagnostic bronchoscope, 9.4%) of *P. aeruginosa* pulmonary infections related to bronchoscope was observed [20]. In 32 infections (66.7%), *P. aeruginosa* was confirmed as the causative organism. The rate of recovery of *P. aeruginosa* from bronchoalveolar-lavage specimens obtained with use of endoscopy-suite bronchoscopes increased from 10.4% at baseline to 31.0% during the outbreak (relative risk, 2.97; 95% CI, 2.28 to 3.90). This large outbreak was apparently caused by a loose biopsy-port cap in the bronchoscopes. The authors concluded that instrument safety and surveillance methods for bronchoscopes must be improved [20].

Suggested prevention measures and their effect on VAP are summarized in *Table 2*.

URINARY TRACT INFECTIONS (UTI) PREVENTION

The urinary tract is responsible for approximately 31% of critically ill patient infections with the presence of a urinary catheter being the major predisposing factor. It is calculated that the incidence of catheter-associated bacteriuria parallels the number of days of catheterization and that the risk of developing bacteriuria increases by 5% each day [21].

General recommendation

Urinary catheters should be inserted only when necessary and left in place only for as long as necessary. For selected patients, other methods of urinary drainage such as condom catheter drainage, suprapubic catheterization, and intermittent urethral catheterization can be useful alternatives to indwelling urethral catheterization.

Hand washing should be done immediately before and after any manipulation of the catheter site or apparatus and catheters should be inserted using aseptic technique and sterile equipment [8].

Closed drainage system

Indwelling catheters should not be changed at arbitrary, fixed intervals.

A sterile, continuously closed drainage system should be maintained.

Recently, a prospective, randomized study on long-term catheterization to investigate whether infection increases with the use of a catheter-valve, compared with the standard drainage system, was performed. In the long-term group the valve was cheaper and caused less morbidity. Since it is constructed to allow one-way flow, it was not associated with an increase in the incidence of UTI [22].

A recent, prospective study on 553 ICU patients in a French hospital, catheterized for more than 48 h, was conducted to verify risk factors for UTI. The new urinary drainage system comprising a preconnected coated latex, a drip chamber, an anti-reflux valve, povidone-iodine-releasing cartridge at the drain port of the urine collection bag, was not efficacious in reducing UTI (46% of patients in the new urinary drainage system did not have bacteriuria compared with 55% with standard urinary drainage system who had bacteriuria, p=NS) [23].

The closed drainage system is widely accepted

TABLE 2 - *Proposed device management for prevention of VAP.*

	Effect on prevention of VAP	Ref.
Educate healthcare workers regarding the invasive procedures	Positive	2
Perform a surveillance program for bacterial pneumonia in ICU	Positive	3,4
Stress hand washing and barrier precautions in healthcare practitioners	Positive	5
Use multi-use, closed-system suction catheters	Positive	6
Sterilize or use high-level disinfection, do not routinely sterilize or disinfect the internal machinery, do not change the breathing circuit routinely, do not place bacterial filters between the humidifier reservoir and the inspiratory-phase tubing of the breathing circuit of a mechanical ventilator	Positive	7,8
Use HME rather than heated humidifiers	Uncertain	9,10, 11,12
Change the hydrophobic or hygroscopic HME after 3 days	Positive	13
Lubricate the cuff of the endotracheal tube with a water-soluble gel to prevent aspiration	Positive	14
Use continuous subglottal suctioning	Positive	15,16
Use Ciaglia method instead of surgical tracheostomy	Uncertain	17
Maintain the semi-recumbent body position in intubated patients	Positive	18
Chest physiotherapy	Positive	19
Improve bronchoscopy safety and surveillance methods	Positive	20

for prevention of UTI. The insertion of a one-way valve does not add more effectiveness to a closed system.

Medicated urinary catheter

Recently, a 12-month, randomized, crossover trial compared rates of nosocomial catheter-associated UTI in patients with silver-coated and uncoated catheters to assess the efficiency of a silver-alloy, hydro gel-coated latex urinary catheter for the prevention of nosocomial catheter-associated UTIs. There were 343 infections in 27,878 patients (1.23 infections per 100 patients) during 114,368 patient-days (3.00 infections per 1000 patient-days). The relative risk of infection per 1000 patient-days was 0.79 (95% CI, 0.63-0.99; P =0.04) for study wards randomized to silver-coated catheters compared with those randomized to uncoated catheters. The conclusion was that the use of the more expensive silver-coated catheter appeared to offer cost savings by preventing excess hospital costs due to nosocomial UTI associated with catheter use [24].

A prospective, randomized, clinical trial was conducted at five academic medical centers on patients undergoing radical prostatectomy. The objective was to examine the efficiency of bladder catheters impregnated with minocycline and rifampin in reducing catheter-associated bacteriuria. The results demonstrated that patients who received the antimicrobial-impregnated catheters had significantly lower rates of Gram-positive bacteriuria than the control group (7.1% versus 38.2%; P <0.001), with similar rates of Gram-negative bacteriuria (46.4% versus 47.1%) and candiduria (3.6% versus 2.9%). So, bladder catheters impregnated with minocycline and rifampin significantly reduced the rate of Gram-positive catheter-associated bacteriuria up to 2 weeks after catheter insertion [25].

In conclusion, the effect of some proposed management methods of urinary catheter on UTI prevention is summarized in *Table 3*.

A NEW VARIABLE: BIOFILM

Biofilm is a new variable. In 1986 Sottile *et al* studied the surfaces of polyvinyl chloride endotracheal tubes removed from 25 ICU patients to determine if bacterial adhesion to those tubes was sufficient to provide a possible source for repeated contamination of the tracheobronchial tract. Of the surfaces studied, 16% were partially covered and 84% were completely covered by an amorphous bacteria-containing matrix. Some biofilm-enclosed bacterial aggregates projected from the matrix into the lumen of the tube [26].

In the same period, using scanning electron

TABLE 3 - *Proposed device management for prevention of UTI.*

Technique	Effect on prevention of UTI	Ref.
Wash hands and use aseptic technique and sterile equipment	Positive	2,8
Use a catheter-valve instead of a standard drainage system	Uncertain	22
Use a catheter-valve with a povidone-iodine releasing cartridge	Negative	23
Use a silver-alloy, hydro gel-coated latex urinary catheter instead of uncoated catheters	Positive	24
Use catheters impregnated with minocycline and rifampin instead of standard bladder catheter	Positive for Gram-positive infection but uncertain for Candida and Gram-negative infection	25

microscopy and culture following scraping and dispersion of biofilm by sonication, the right heart flow-directed catheters were also found to be covered by a biofilm, with bacteria visible on 75% of them, an average of 2.6 days after insertion [27].

Biofilm is an assemblage of microbial cells that is irreversibly associated with a surface and enclosed in a matrix of primarily polysaccharide material [28]. Biofilm-associated microorganisms differ from their planktonic (freely suspended) counterparts with respect to the genes that are transcribed. There are several modifications of cell properties: hydrophobicity, presence of fimbriae and flagellae and production of extracellular polymeric substances that influence the rate and extent of attachment of microbial cells [28].

The bacteria and fungi that most frequently produce biofilm commonly associated with ICU infections are: *Staphylococcus aureus, Pseudomonas aeruginosa*, coagulase-negative staphylococci, *Enterococcus* spp, *Klebsiella pneumoniae*, and *Candida albicans* [28]. Biofilm may form on a wide variety of surfaces: living pathological tissues [29], indwelling medical devices, industrial water system piping or natural water systems [28].

The relationship between endotracheal tube (ET) biofilm and pulmonary pathogens in VAP was demonstrated in an investigation where the same microorganisms were found on tracheal and ET samples by phenotype, confirmed as identical by genotyping, and characterized for antibiotic susceptibility in both the free-floating and biofilm forms. Seventy per cent of patients with VAP had identical pathogens isolated from both ET biofilm and tracheal secretions. Susceptibility data for these pairs show that the ET acts as a reservoir for infecting microorganisms, which exhibit significantly greater antibiotic resistance than their tracheal counterparts [30].

Bacteria in biofilm are less exposed and more resistant to the action of antimicrobial drugs [31].

The factors associated with bacterial biofilms were studied for their role in phenotypic resistance to antibiotics [31]. These factors included bacterial slime extracted from biofilm, reduced growth rates of biofilm-embedded bacteria and high bacterial inocula. Antibiotic activity against suspended bacteria in the presence of these factors, either alone or combined, was compared with activity against adherent biofilms. All minimal inhibitory concentrations (MICs), determined by standard susceptibility tests, were below the sensitivity breakpoints for *Staphylococcus epidermidis*. The addition of bacterial slime to suspended bacteria reduced the bactericidal activity of glycopeptides but had less or no effect on the activity of the other antibiotics tested [31].

Therefore, new therapeutic strategies are needed to reduce the impact of biofilm infections in ICUs. The first strategy that has produced some results is the administration of gentamicin by aerosol in intubated patients with VAP. Adair *et al.* compared the efficacy of gentamicin, nebulized via the ET, with that of parenteral cefotaxime or parenteral cefuroxime in preventing the formation of ET biofilm in 36 patients at risk for VAP. They concluded that nebulized gentamicin attained high concentrations in the ET lumen and was more effective in preventing the formation of biofilm than either parenterally-administered cephalosporin and therefore may be effective in preventing this complication of mechanical ventilation [32].

The capacity of bacteria to organize a biofilm on a device surface and the related resistance to antimicrobial drugs can explain the difficulty in eradicating an infection in the ICU even when antibiotic therapy seems to be adequate.

CONCLUSIONS

There are a large number of clinical trials in the literature but with many uncertain results and often reports of no difference in the benefits offered by each intervention. There is a need for more studies on greater numbers of patients to establish significant differences among procedures and products.

Since manufacturers often argue that their device is superior to an alternative, and promote clinical trials, results can be impartial. Studies on prevention of device-related infections are difficult to carry out and expensive but they are needed to verify the efficacy of prevention measures for device-related infections in the ICU.

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