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ORIGINAL ARTICLE

Frequency of Ventilator-associated Pneumonia With 3-day Versus 7-day Ventilator Circuit Changes

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Background: Ventilator-associated pneumonia (VAP) is a common clinical problem. Previous studies involving adult patient cohorts have assessed various risk factors associated with VAP, including ventilator circuit changes. The objective of this study was to examine the incidence of and risk factors associated with VAP, particularly 3-day versus 7-day ventilator circuit changes, in a pediatric intensive care unit (PICU).
Methods: This was a cohort observational study. Patients hospitalized in the PICU at Chang Gung Children's Hospital between November 2003 and September 2004 were enrolled. Investigators and critical-care specialists evaluated baseline characteristics, incidence of VAP, and related variables from PICU admission until discharge or death.
Results: Of 397 patients initially enrolled, 96 (aged 11–60 months) were available for statistical analysis and were assigned into two groups according to timing of ventilator circuit change: 3-day (n=46) and 7-day circuit change (n=50). No statistically significant differences were observed for VAP incidence (13% *vs*. 16%, p=0.68) or hospital mortality (22% *vs*. 36%, p=0.14) for 3-day versus 7-day circuit change. Incidence of VAP per 1000 ventilation days was 10.75 and 8.41 for 3-day and 7-day circuit change, respectively. Univariate analysis indicated statistical significance for the duration of mechanical ventilation (10.17±16.63 days *vs*. 18.20±14.99 days, p<0.001), length of stay in PICU (22.30±20.48 days *vs*. 37.22±36.79 days, p=0.0069) and presence of enteral nutrition [7 (15.22%) *vs*. 23 (46.0%), p=0.0012].
Conclusion: Weekly circuit change does not contribute to increased rates of VAP in pediatric patients. Long-term studies evaluating risk factors in larger pediatric patient populations are warranted for further conclusive recommendations.

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1. Introduction

Ventilator-associated pneumonia (VAP) is a nosocomial infection occurring ≥48 hours after instituting mechanical ventilation. Pharyngeal colonization results in circuit colonization.[1,2] The known causative factors of VAP include contaminated ventilator tubing condensate, reduced gastric activity as a result of antibiotic therapy, stress ulcer prophylaxis, supine head positioning, parenteral nutrition, nasogastric intubation and poor hand washing.[3–6] The 2006 US National Healthcare Safety Network (NHSN) data summary reported a pooled mean incidence of VAP at pediatric intensive care units (PICU) of 2.5 per 1000 ventilator days.[7] The incidence of VAP varies worldwide, ranging from 1.7 to 8.9 per 1000 ventilator days. While blood stream infections are the most common nosocomial problem in the PICU, VAP is the infection with the highest mortality rate, at 8%, for deaths directly attributable to VAP.[8,9]

Studies evaluating correlations between respiratory equipment and the development of VAP have proposed the biofilm in endotracheal tubes and ventilator circuit changes as possible contributing factors. While one study in neonates failed to demonstrate a correlation between the presence of the film and nosocomial infection, another study showed that 70% of pathogens recovered from the endotracheal tube were genotypically the same as those recovered from tracheal secretions in patients with VAP.[10–12] Thus, whether endotracheal tubes and biofilm are risk factors for VAP or not has yet to be determined.

The other factor associated with VAP is the frequency at which ventilator circuit is changed. Currently, maintaining circuit integrity with less frequent circuit changes, with or without a heat-and-moisture filter, is preferred and prevents the introduction of nosocomial pathogens. Cost savings are an additional benefit resulting from the reduced use of disposable equipment and circuit maintenance.[13–15] Guidelines from the American Association of Respiratory Care on the care of ventilator circuits recommend that the "Ventilator circuit should not be changed routinely for infection control purposes [as] available evidence suggests that no patient harm and considerable cost savings are associated with extended ventilator-circuit change intervals. The maximum duration of time that circuits can be used is not known."[16] However, most of the current practices and conclusions are based on studies in adult patients with necessity-based ventilator use and interventions designed to accelerate weaning from mechanical ventilation, including early extubation, use of non-invasive ventilators and weaning protocols.[17,18]

The incidence of VAP in pediatric populations and the relationship between VAP and frequency of ventilator circuit change have been less extensively studied. Large neonatal intensive care units (ICUs) in the United States prescribe ventilator circuit changes every 2–7 days.[19] Prior to this study, a 3-day ventilator circuit change was routine in our PICU. The objective of this study was to measure the incidence of VAP within a PICU in a teaching hospital and to observe if there was a difference in incidence of VAP and mortality in patients on a 3-day versus 7-day ventilator circuit change regimen.

2. Materials and Methods

2.1. Study location and patients

We conducted this observational study between November 2003 and September 2004 at the Chang Gung Children's Hospital, which has a 29-bed PICU staffed by two pediatric critical care intensivists, two pediatric critical care fellows, one pediatric cardiologist, one pediatric cardiology fellow, and two 3rd-year residents. Patients were cared for by the attending physicians and residents rotating on a weekly or monthly basis, with a maximum nurse-to-patient staffing ratio of 1 to 3. Eligible patients were those that required ventilator support with primary endotracheal intubation performed within the PICU. The exclusion criteria were, (1) patients extubated or who died within 72 hours of admission; (2) pre-existing artificial airway/tracheostomy and/or ventilator use at admission; (3) non-invasive ventilator use (bi-level positive airway pressure or continuous airway pressure); (4) premature circuit change; (5) pneumonia diagnosed prior to intubation. Premature circuit change was defined as a circuit change made before the scheduled date, according to the protocol, due to severe circuit air leak, endotracheal tube obstruction, or grossly solid condensate deposited in the circuit. All study protocols were performed in accordance with previous guidelines prescribed by the director of pediatric critical care and emergency medicine and the Institutional Review Board at Chang Gung Children's Hospital.

2.2. Study design and data collection

This was an observational cohort study. We divided the admitted children on a chronologic basis. Patients who were admitted between November 1, 2003, and April 30, 2004, received ventilator circuit changes every 3 days. Patients who were admitted between May 1, 2004 and September 30, 2004, received ventilator circuit changes every 7 days. The ventilators

used were Siemens Servo 300 (Siemens-Elema, Solna, Sweden), Puritan-Bennett 7200 (Nellcor Puritan Bennett, Pleasanton, CA, USA), VIB Bird and HFOV-SensorMedics 3100A, B (Viasys Healthcare, Yorba Linda, CA, USA). The ventilator circuits (Hytrel Tube; Fisher and Paykel Co., Irvine, CA, USA) included gas delivery tubing, humidifier water reservoirs, water traps and medication delivery devices. All ventilator circuits were disposable, equipped with a Y-connector, and contained an attached trap to collect tubing condensate. Ventilator circuits were changed at any time at the discretion of the individual physicians or the respiratory therapists. Patients transferred for surgical intervention, while in the PICU, received the same ventilator and circuit upon return to the PICU to minimize unscheduled circuit changes. Ventilator circuits were monitored at least once every 2 hours and water traps were emptied when filled.

Upon admission, demographic and baseline characteristics were collected; these included age, sex, presence of concomitant systemic underlying disease(s), and Pediatric Risk of Mortality (PRISM) score. Concomitant systemic underlying disease was defined as the presence of congenital heart diseases, bronchopulmonary dysplasia, severe central nervous system diseases or myopathy, severe hereditary metabolic or chromosomal diseases, malignancy, or post-transplant status. Medical or surgical interventions during admission thought to predispose patients to VAP, including transfusions, type 2 histamine receptor antagonist or proton pump inhibitors, tracheostomy, fiberscopy (pandoscopy or bronchoscopy) and extracorporeal circuit use (such as extracorporeal membrane oxygenation and continuous renal replacement therapy) were also recorded.

The primary outcome was incidence of VAP. Secondary outcomes were hospital mortality, length of PICU stay, total number of ventilation days for a single intubation, successful extubations, and deaths directly attributable to VAP. The study patients were monitored for occurrence of VAP on a daily basis until successful extubation in the PICU or death.

2.3. Definitions

PRISM is a validated, generic, mortality scoring system counted during a 24-hour observation period for children admitted to PICUs.[20]

The diagnostic protocols for VAP were applied in accordance with criteria prescribed by the NHSN.[21] PICU flow sheets were reviewed daily, in conjunction with microbiological culture and radiology results, to determine pneumonia.

A diagnosis of pneumonia was established according to the NHSN algorithm for clinically defined pneumonia when one of the following was observed on radiographic analysis: new or progressive and persistent infiltrate lasting >48 hours; consolidation; or cavitation with any of the following: (1) fever ($>38^{\circ}$C or $>100.4^{\circ}$F) with no other recognized cause; (2) leukocytes $\geq 12.0\times10^6$/L or leukopenia with leukocytes $<4.0\times10^6$/L; (3) worsening gas exchange with O_2 desaturation ($PaO_2/FiO_2 \leq 240$), increased oxygen requirements, or increased ventilator demand; (4) new onset of purulent sputum, defined as the presence of 25 leukocytes and <10 squamous cells per high power ($100\times$) field; or (5) new onset of cough, dyspnea or tachypnea.

Microorganisms were determined by endotracheal aspirate culture. VAP cases were further divided into early-onset VAP (occurring <5 days of mechanical ventilation) and late-onset VAP (occurring ≥ 5 days of mechanical ventilation).[22]

2.4. Statistical analysis

Demographic data are presented as means and standard deviation, median and interquartile range, and frequency/percentage in parentheses. Univariate comparisons were made using Wilcoxon rank sum and χ^2 tests, depending on statistical distributions. Log-rank tests for equality of survival curves across strata and multivariate logistic regression were used to evaluate incidence of VAP. All data were analyzed using SAS version 9.0 (SAS Institute Inc., Cary, NC, USA), and significance level was 0.05. Power analysis, computed *a priori* with STPLAN version 4.2 (University of Texas, MD Anderson Cancer Center, Houston, TX, USA) was based on differences in the incidences of VAP. Preliminary estimates of the incidence showed that a sample size of 45 per group would yield a power of 80% to detect a difference of at least 0.05 in the incidence of VAP between the two comparison groups, assuming a 5% level of significance.

3. Results

A total of 397 patients were enrolled in the study (Figure 1). Of these, 192 patients were enrolled in the 3-day circuit change group while 205 patients were enrolled in the 7-day circuit change group according to the time of admission. Fifty-five patients (3-day group, $n=22$; 7-day group, $n=33$) were excluded due to non-invasive ventilator use. Another 176 patients (3-day group, $n=94$; 7-day group, $n=82$) were subsequently excluded due to pre-existing artificial airway use in a previous PICU admission. Further screening resulted in 76 patients in the 3-day circuit change group and 90 in the 7-day group. Sixteen patients in the 3-day group and 27 patients

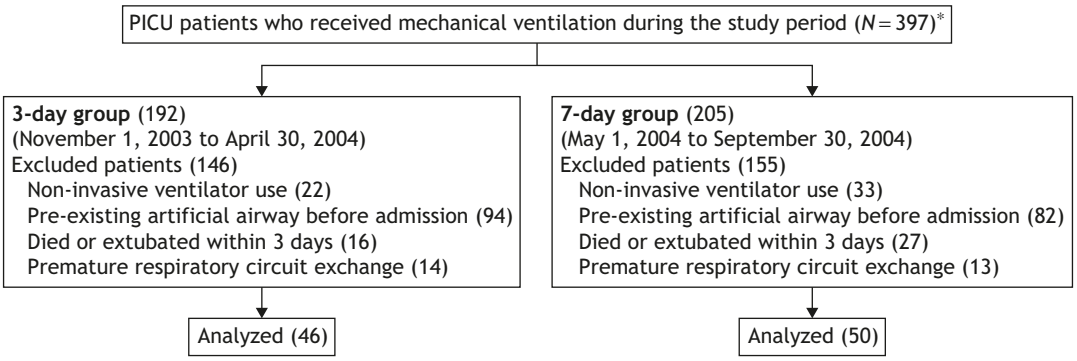

Figure 1 Study flowchart. *Number of cases is expressed as (*n*). PICU = pediatric intensive care unit.

Table 1 Baseline characteristics of patients allocated to the 3-day and 7-day circuit change

Characteristics	3-day change (*n* = 46)*	7-day change (*n* = 50)*	*p*†
Age (mo)‡	39.93 ± 43.76 21.50 (11.0–52.0)	52.54 ± 61.14 27.00 (7.0–60.0)	0.82
Male	24 (54.4%)	27 (54.0%)	0.97
Presence of concomitant underlying systemic disease on admission	29 (63.0%)	33 (66.0%)	0.76
PRISM score‡	13.0 ± 5.8 12 (9–16)	13.5 ± 7.1 18 (13–21.5)	0.50
Mechanical ventilation duration (d)‡	10.17 ± 16.63 5 (4–10)	18.20 ± 14.99 14.5 (8–22)	< 0.001§
Length of PICU stay (d)‡	22.3 ± 20.5 17 (8–28)	37.2 ± 36.8 27 (15–51)	0.007§
Successful extubation	36 (78.3%)	32 (64.0%)	0.13
H2-blocker use and/or proton pump inhibitor	19 (41.3%)	18 (36.0%)	0.59
Parenteral nutrition	7 (15.2%)	23 (46.0%)	0.001§
Fiberscopy	9 (19.6%)	18 (36.0%)	0.07
Tracheostomy	2 (4.3%)	5 (10.0%)	0.44
Transfusion	21 (45.7%)	28 (56.0%)	0.31
Extracorporeal circuit use‖	4 (8.7%)	6 (12.0%)	0.60

*Data are presented as *n* (%), mean ± standard deviation or median (interquartile range); †χ^2 test; ‡Wilcoxon rank sum test; §$p < 0.05$; ‖extracorporeal circuit use includes hemodialysis, continuous renal replacement therapy, continuous arterio-venous hemofiltration or extracorporeal membrane oxygenation. PRISM = Pediatric Risk of Mortality; PICU = pediatric intensive care unit.

in the 7-day group died or were extubated within 3 days. Fourteen patients in the 3-day group and 13 in the 7-day group were excluded due to premature circuit change. Finally, the 3-day circuit change group comprised 46 patients and the 7-day circuit change group 50 patients.

The baseline characteristics are shown in Table 1. Of the 96 patients in both groups, 52.2% (24/46) of the 3-day group and 54.0% (27/50) of the 7-day group were males. Both study groups were similar in age (3-day *vs.* 7-day, 39.93 ± 43.76 months *vs.* 62.54 ± 61.14 months, $p = 0.818$). The incidence of concomitant underlying systemic disease was low in both groups. Specific medical and/or surgical interventions during PICU admission were similar in both groups except for parenteral nutrition use [7 (15.2%) *vs.* 23 (46.0%), $p = 0.001$].

The two variables that were significantly different between the two groups are the total duration of mechanical ventilation (10.17 ± 16.63 days *vs.* 18.20 ± 14.99 days, $p < 0.001$) and the length of stay in PICU (22.30 ± 20.48 days *vs.* 37.22 ± 36.79 days, $p = 0.007$).

As shown in Table 2, VAP occurred in six (13.0%) patients in the 3-day group and eight (16.0%) patients in the 7-day group. In the 3-day group, three patients had positive sputum cultures (oxacillin-resistant *Staphylococcus aureus*, enterobacter and pseudomonas), while in the 7-day group, five had positive sputum cultures [*Escherichia coli* (1),

Table 2 Correlation between ventilator-associated pneumonia and circuit change frequency

Variable	3-day change (n=46)*	7-day change (n=50)*	p
Number of patients with VAP[†]	6 (13.0%)	8 (16.0%)	0.68
Duration of VAP (d)[‡]	14.5 (4–17)	10 (4–16)	0.62
Hospital mortality[§]	10 (21.7%)	18 (36.0%)	0.14
Deaths directly related to VAP[‖]	1 (10.0%)	6 (33.3%)	0.13
Ventilation days (total)[‡]	113	200	0.05
VAP/1000 ventilation days	10.75	8.41	0.33

*Data are presented as n (%) or median (interquartile range); [†]compared with χ^2 tests; [‡]compared with Wilcoxon rank sum test; [§]compared with log-rank test for time to death in hospital and the denominator is the number of subjects assigned to each group; [‖]compared with log-rank test for time to VAP death and the denominator is hospital mortality. VAP=ventilator-associated pneumonia.

Klebsiella oxytoca (1), oxacillin-resistant *Staphylococcus aureus* (1), and pseudomonas (3)]. Early-onset VAP occurred in 66.7% (4/6) and 50.0% (4/8) of patients who developed VAP in the 3-day and 7-day groups, respectively. There were 10 (21.7%) and 18 (36.0%) mortalities in the 3-day and 7-day groups. Deaths related to VAP occurred in 10.0% (1/10) and 33.3% (6/18) of patients in the 3-day and 7-day groups, respectively. The total duration of ventilation was 113 days for the 3-day group and 70 days for the 7-day group. Incidence of VAP per 1000 ventilation days was 10.75 and 8.41, respectively. No statistical significance was observed for these variables ($p>0.05$). A multivariate logistic model was developed to evaluate the VAP rate after adjusting for the total duration of mechanical ventilation and length of stay in PICU (not shown). However, no significant difference between the two groups were found ($p=0.63$).

4. Discussion

This was an observational cohort study focusing on the relationship between the frequency of ventilator circuit change and VAP in the PICU setting. We found that extending the use of ventilator circuit from 3 days to 7 days did not significantly affect VAP incidence or contribute to deaths related to VAP ($p>0.05$) in our PICU. The difference between VAP occurrence and deaths between the two groups might be attributable to more patients enrolled in the 7-day circuit group who later developed multiple organ failure during their PICU stay. However, the results of this study cannot statistically confirm the conventional opinion that extending the circuit change intervals from 3 days to 7 days reduces the rate or risk of VAP.[13,14,23,24]

Four limitations may have compromised the statistical integrity of the study. Firstly, the PRISM score did not reflect the "exact" illness severity during the entire PICU course. Secondly, the scheduled difference between the 3-day and 7-day ventilator circuit change groups may inherently affect the length of time for mechanical ventilation (i.e., the 7-day group had longer baseline mechanical ventilation days). Thirdly, we did not use protocol-driven weaning profiles, such as daily testing of patient readiness for extubation, and the individual physician decision bias may have influenced mechanical ventilation duration and even length of stay in PICU. Lastly, we did not strictly adhere to the VAP preventative procedure, which may have reduced overall VAP incidence substantially.

Seasonal variations may also affect the pattern of PICU admission because in winter time, respiratory diseases tend to contribute to more admissions while in summer time, enteroviral infections tend to contribute to more admissions. However, in our study, we did not see perennial variations in the basic characteristics of our enrolled patients. There were two reasons that might explain this. Firstly, we excluded cases with diagnosed pneumonia prior to PICU admission during the initial enrollment. This step likely reduced the seasonal admission variation. Secondly, we excluded cases with a pre-existing artificial airway, previous ventilator use, or non-invasive ventilator use during enrollment. Together, these represent a diverse range of inherent endemic risks that we wanted to avoid during this study.

Until the 1990s, contamination of respiratory support equipment was considered a significant source of nosocomial respiratory tract infection.[25] It is now clear that routine, frequent changes of the ventilator circuit are not necessary in neonatal or adult ICUs.[1,15,19] Results of the current study are in agreement with other studies to date.[1,13,15,19,26] Dreyfus et al[1] in a randomized study, found no difference in the incidence of VAP between 2-day and 7-day circuit changes with heated humidification. Similarly, Hess et al[26] when compared 2-day with 7-day circuit changes in 3423 adult patients, found

no difference in the incidence of VAP (5.6% *vs.* 4.6%). Kollef et al[15] studied having no routine circuit changes versus 7-day circuit changes, but noted no difference in VAP occurrence between the two groups, with a non-significant relative risk of 0.85 (95% confidence interval: 0.55–1.17). In one of the few studies examining neonatal population, Makhoul et al[19] examined the incidence of VAP in premature infants following circuit changes of 1 day versus 3 days. They reported that increasing the frequency of circuit change from 1 day to 3 days did not increase the occurrence rate of VAP, and reported no statistically significant difference in duration of hospitalization and hospital mortality between the two groups.[19] Meta-analysis of the same data however, revealed a reduced odds ratio (0.82, $p=0.22$) for developing VAP in the 7-day circuit change group.[13]

In contrast, some studies have also found significant differences when the frequency of circuit change was varied.[14,23,27,28] Fink et al[14] assessed circuit changes at 2 days, 7 days and 30 days in a study conducted between January 1991 and December 1994. They found that the incidence of VAP per 1000 ventilator days was 11.88, 3.42 and 6.28 for 2-day, 7-day and 30-day circuit changes, respectively.[14] Han et al[23] and Lien et al[27] compared 2-day with 7-day circuits in two separate studies and found a reduction in VAP rate from 9.2% to 3.5% in the 7-day group but Lien et al found no difference in the VAP rate (2.9% *vs.* 3.2%) between the two groups. Stamm[28] reviewed six studies that compared the VAP rates with 2-day versus 7-day circuit changes and found that the evidence supported less frequent circuit changes.

With regard to the issue of why more frequent circuit changes could lead to higher incidence of VAP, Craven et al[5] and the American Association of Respiratory Care guidelines[16] proposed that "breaking the circuit" may result in flushing contaminated tubing condensate into the patient or increasing the lavage of bacteria into the trachea from around the endotracheal tube due to unnecessary manipulation of the patient, endotracheal tube or ventilator tubing. The Centers for Disease Control and Prevention recommends routine ventilator circuit changes for grossly visible contamination of the circuit with blood, emesis or purulent secretions.[29] These measures may not only reduce the overall VAP occurrence rates and exposure of patients and healthcare providers to infectious aerosols, but also lower the cost and labor associated with frequent circuit changes.

In terms of cost-effectiveness, Hess[26] reported that 7-day circuit changes reduced annual costs incurred for maintenance and salaries by 76.6% (US$113,530). In Taiwan, we could not calculate the total cost associated with respiratory circuit exchange because of the bundled payment system for mechanical ventilation. However, the positive effect on resource conservation should be substantial in the absence of costs attributed to an increase in VAP.

When compared with adults, intubated children supported on mechanical ventilation have similar and unique risk factors for developing VAP. Similar risks include aspiration or oropharyngeal or gastric secretions. Unique risks include incomplete dentition and use of uncuffed endotracheal tubes.[30] Additional risk factors in adults include the duration of mechanical ventilation and prolonged ICU stay.[3,6,31] We found that duration of mechanical ventilation and length of stay in PICU were significant risk factors for the development of VAP, similar to findings reported by Edwards et al.[32] They noted that the 34 patients who had VAP (out of 595 mechanically ventilated patients) had longer length of stay in PICU (27.53 ± 20.09 days, $p=0.001$). They also addressed two risk factors not specifically assessed in our study, namely higher mean PRISM score and longer duration of hospital stay.[32]

In this study, the incidence of VAP per 1000 ventilator days was 10.75 and 8.41 for 3-day and 7-day circuit changes, similar to the upper average reported in the literature.[9] Edwards et al[32] reported a pooled mean VAP of 11.6 cases per 1000 ventilator days. The results of the current study may be related to several factors in our PICU: a high prevalence of prolonged multiple antibiotic use, reduced adherence to hand-washing, absent routine in-line suction, and less strict use of the semi-recumbent position rather than the supine position. Brilli et al[33] reported that implementing specific VAP-preventative measures with a checklist of actions and tasks in a PICU setting significantly reduced the VAP rates from 6.6 cases per 1000 ventilator days to 0.5 cases per 1000 ventilator days ($p<0.05$), suggesting that implementing and adhering to such measures could significantly reduce the incidence of VAP.

Given the paucity of specific pediatric research, many low-risk practices validated in the adult population are implemented in the pediatric critical care setting without appropriate testing. We performed this observational study so as to obtain direct evidence for less-frequent circuit changes. Results of the current study confirm that prolonging the time between VAP circuit changes from 3 days to 7 days in the PICU does not contribute to the incidence of or mortality due to VAP, similar to results from adult ICU studies. In recent years, strict VAP preventative procedures have been implemented in adult ICUs and in some PICU settings, resulting in a significant reduction in the incidence of VAP and reduced treatment costs.[30,33] Further research is warranted to prospectively evaluate VAP preventative procedures in PICU settings.

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