



Original article

Risk factors for ventilator-associated pneumonia in neonatal intensive care unit patients



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ABSTRACT

Ventilator-associated pneumonia (VAP) is a serious complication in neonatal patients on mechanical ventilation. The objective of this study was to examine the incidence and risk factors associated with VAP, particularly in every 7-day versus every 14-day ventilator circuit changes, in a neonatal intensive care unit (NICU). Seventy-one neonates hospitalized in the NICU were enrolled. First, the neonates were divided into groups with and without VAP. On univariate logistic regression analyses, prolonged mechanical ventilation, frequent re-intubation, low gestational age, and low birth weight (BW) were significant risk factors for VAP development. After adjustments for other variables, only BW <626 g was a significant independent predictor for VAP in NICU infants. Second, to examine the effect of the frequency of changing ventilator circuits on the incidence of VAP, circuit changes were compared between the every 7-day group and the every 14-day group. The incidence of VAP per 1000 ventilator days was 9.66 for the every 7-day group and 8.08 for the every 14-day group, and there was no significant difference between the 2 groups. BW <626 g was a significant independent predictor of VAP, and decreasing the frequency of ventilator circuit changes from every 7 days to 14 days had no adverse effect on the VAP rate in the NICU.

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1. Introduction

Ventilator-associated pneumonia (VAP) is pneumonia in mechanically ventilated patients that develops later than or at 48 h after the patient has been placed on mechanical ventilation [1–5]. VAP is a serious complication in neonates on mechanical ventilation and the second most common hospital-acquired infection among neonatal intensive care unit (NICU) patients [1–9]. Whereas the severities of the underlying disease and the acute illness of adult patients with VAP are known to contribute to poor outcomes, there are limited data with respect to the incidence, characteristics, risk factors, and outcomes of VAP in neonates. In a meta-analysis of

observational studies, Tan et al. identified ten variables as independent risk factors for the development of VAP: length of stay in the NICU, re-intubation, enteral feeding, mechanical ventilation, transfusion, low birth weight, premature infants, parenteral nutrition, bronchopulmonary dysplasia, and tracheal intubation [9]. A study in pediatric ICU (PICU) patients identified genetic syndromes, re-intubation, and transport out of the PICU as independent risk factors for VAP in neonates [10]. Because neonates have different anatomy, physiology, and underlying diseases, and they undergo different invasive procedures compared with adults and older children, specific studies of risk factors and outcomes for neonatal VAP are needed [7]. Routine circuit changes are not recommended in the Centers for Disease Control and Prevention (CDC) guideline 2003 [1] and by the European Task Force [2] and the American Thoracic Society [3]. No routine circuit change seems safe and justified in adults [5].

On the other hand, there is a small number of studies about VAP in neonatal infants [7,8]. Samransamruajkit et al. reported that

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7-day ventilator circuit change did not contribute to increased rates of VAP in the PICU in a prospective study [11], and no routine circuit change was also recommended for neonatal patients in Japan [4]. However, there was no evidence about extending the ventilator interval from 7 days to 14 days or more in the NICU. The objective of this study was to examine the risk factors associated with VAP, particularly 7-day versus 14-day ventilator circuit changes, in the NICU.

2. Patients and methods

This was a retrospective observational study. All neonates with birth weight ≤ 2000 g admitted to the NICU between January 2009 and June 2012 on a ventilator for ≥ 48 h were included in the study. The interval of ventilator circuit changes was changed from every 7 days to every 14 days on July 1st, 2011 in the NICU at Osaka Medical College Hospital. Thus, period 1 with 7-day ventilator circuit changes was from January 1st, 2009 to June 30th, 2011, and period 2 with 14-day ventilator circuit changes was from July 1st, 2011 to June 30th, 2012. To establish the oral resident flora in neonates, the infants' mouths were smeared with breast milk early after birth, and the neonates were nursed with mother's milk as much as possible in our NICU [4]. Oral care was performed, and a closed system suction catheter for multiple-time use was used in all cases [4,12]. Post-pyloric tube feeding was used for enteral nutrition, if possible, because it has been suggested that placement of a post-pyloric tube can reduce the risk of aspiration and VAP [4,12].

VAP was diagnosed by two pediatricians using criteria for ≤ 1 -year-olds established by Foglia et al. [7]. The criteria were as follows. Neonatal patients who are mechanically ventilated for more than or equal to 48 h must have new onset abnormal chest radiographs and worsening gas exchange (oxygen desaturations, increased oxygen requirements, or increased ventilator demand) and at least three of the following: temperature instability with no other recognized cause; new onset of purulent sputum, change in character of sputum, increased respiratory secretions, or increased suctioning requirements; apnea, tachypnea, nasal flaring with retraction of the chest wall, or grunting; wheezing, rales, or rhonchi; cough; and bradycardia (< 100 beats/min) or tachycardia (> 170 beats/min).

First, to examine the incidence and risk factors associated with VAP, the neonates were divided into groups with and without VAP, and univariate logistic regression analysis and adjustments for other variables were performed. Sex, Apgar score at 1 min, Apgar score at 5 min, body weight, gestational age (GA), period 1 or 2, caesarean birth, days in incubator, days with ventilator, and tube changes (times) were analyzed. Patients with circuit changes because the circuit was visibly soiled or mechanically malfunctioning were excluded.

Second, to examine the effect of the frequency of changing ventilator circuits on the incidence of VAP, circuit changes every 7 days in period 1 and every 14 days in period 2 were compared. Patients on a ventilator for 14 days or more were enrolled during the whole period.

The study protocol was approved by the Institutional Review Board of Osaka Medical College. All data were anonymized before statistical analysis. Data are expressed as means \pm standard deviation (SD), medians with quartile range (25–75%), or numbers with percentage. NICU infants were classified into two groups, with and without VAP. Continuous variables in the two groups were compared by the unpaired *t*-test or the Mann–Whitney *U*-test according to the data distribution. Categorical variables were compared between two groups using Fisher's exact test. Binary logistic regression analyses were conducted to identify predictors for the onset of VAP in NICU patients. When collinearity between

Table 1
Characteristics of NICU infants with and without VAP.

	All cases	With VAP	Without VAP	P values
	(n = 71)	(n = 11)	(n = 60)	
Male (%)	28 (39.4)	4 (36.4)	24 (40.0)	0.999 ^a
Apgar score 1 min	4.0 [2.0–6.0]	3.0 [1.5–4.0]	4.0 [2.0–6.3]	0.074 ^b
Apgar score 5 min	7.0 [6.0–8.0]	6.0 [5.5–7.5]	7.0 [6.0–8.3]	0.173 ^b
Body weight (g)	1122 \pm 686	501 \pm 227	1236 \pm 682	< 0.001 ^c
GA (weeks)	29.2 \pm 4.6	27.2 \pm 3.7	29.6 \pm 4.7	0.115 ^c
Cesarean birth (%)	54 (76.1)	7 (63.6)	47 (78.3)	0.441 ^a
Period 1 (%)	31 (43.7)	5 (45.5)	26 (43.3)	0.999 ^a
Days in incubator	50 [23–71]	65 [50–90]	49 [22–69]	0.115 ^b
Days on ventilator	13 [4–33]	56 [33–64]	9 [4–24]	< 0.001 ^b
Tube change (times)	0.0 [0.0–1.0]	3.0 [1.5–4.0]	0.0 [0.0–1.0]	< 0.001 ^b

Data are expressed as numbers (%) or medians [25%–75%] or means \pm SD. NICU, neonatal intensive care unit; VAP, ventilator-associated pneumonia; GA, gestational age.

^a P values were determined by Fisher's exact test.

^b Mann–Whitney *U*-test.

^c Unpaired *t*-test.

two variables was evident, each of them was excluded from a multiple logistic regression model. A receiver operating characteristic (ROC) curve analysis was used to confirm the accuracy of the binary logistic regression model and to determine the cut-off values of explanatory variables as predictors for the onset of VAP in NICU patients. All statistical analyses were performed using IBM SPSS, version 18. A *P* value < 0.05 was considered significant.

3. Results

A total of 71 (31 in period 1 and 40 in period 2) neonates hospitalized in the NICU at Osaka Medical College Hospital between January 2009 and June 2012 was enrolled. Fourteen VAP episodes developed in 11 patients, and the rate of VAP per 1000 ventilator days was 8.44 during the whole period. No outbreaks with multi-resistant bacteria occurred during the whole period. The neonates were divided into the with VAP group ($n = 11$) and the without VAP group ($n = 60$) (Table 1). Most patients were premature, and all were in incubators and treated with a ventilator. Body weight in 80% (57/71) of infants was < 1500 g, and GA in 62% (47/71) of infants was < 30 weeks. In the comparison between the with and without VAP groups, body weight was significantly smaller in the with VAP group, and days on ventilator and times of ventilator tube changes were significantly greater in the with VAP group

Table 2
Predictors for the onset of VAP in NICU infants: Binary logistic regression analyses before and after adjustments.

Variables	Univariate analysis		Multivariate analysis	
	OR (95%CI)	P values	OR (95%CI)	P values
AS at 1 min < 4 points	2.82 (0.74–10.69)	0.128	NA	
BW < 626 g	40.50 (7.05–232.82)	< 0.001	21.06 (2.64–168.19)	0.004
GA < 24.6 weeks	3.38 (0.70–16.26)	0.129	NA	
Incubator use ≥ 50 days	3.05 (0.74–12.62)	0.124	NA	
Ventilator use ≥ 26 days	14.79 (2.85–76.59)	0.001	2.67 (0.21–33.83)	0.449
Tube change ≥ 1 time	7.77 (1.54–39.26)	0.013	1.16 (0.10–14.03)	0.907

Determination coefficient: $r^2 = 0.404$ ($P < 0.001$). The chi-square value is 0.586, and $P = 0.900$ as determined by the Hosmer–Lemeshow test.

VAP, ventilator-associated pneumonia; NICU, neonatal intensive care unit; OR, odds ratio; CI, confidence interval; AS, Apgar score; BW, body weight; GA, gestational age; NA, not applicable.

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