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Concise Communication

Polymyxin flushes for endotracheal tube suction catheters in extremely low birth-weight infants: Any benefit in preventing ventilator-associated events?

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Abstract

We report that receipt of polymyxin B endotracheal tube suction catheter flushes did not reduce the incidence of pediatric ventilator-associated events (PedVAE) in infants weighing <1,000 g in this retrospective study. Incidence of PedVAE in our group of extremely low birth-weight infants was 6 per 1,000 ventilator days.

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Ventilator-associated complications are a significant cause of morbidity and mortality among neonates in the intensive care unit and lead to increased patient ventilator days and length of stay.[1,2] Existing literature on prevention of neonatal ventilator-associated complications is limited, and reports are often based on subjective event definitions.

Oropharyngeal administration of antibiotics has been shown to reduce bacterial growth in tracheal cultures in very low birth-weight neonates.[3] Polymyxin administration into endotracheal (ET) tubes has been used as part of neonatal selective aero-digestive tract decontamination protocols[4] and topical pharyngeal antibiotic regimens.[3]

In this study, we examined the use of polymyxin solution flushes of the endotracheal tube suction catheter and rates of pediatric ventilator-associated events (PedVAE) in extremely low birth-weight infants.

Methods

Study design and setting

We conducted a single-center, retrospective, cohort study of infants on first admission to the neonatal intensive care unit (NICU) weighing <1,000 grams who were on mechanical ventilation for at least 3 consecutive days between January 1, 2015, and April 4, 2017. Normal saline flushes are used for routine airway suction and clearance for intubated infants in the NICU. The NICU protocol for management of infants weighing <1,000 g included the optional use of polymyxin B sulfate 500 units/3 mL solution flushes of the endotracheal tube suction catheters in place of saline, wherein a single dispensed dose of polymyxin was used for multiple suction catheter flushes over the course of a nursing shift and flushes were performed as needed. In practice, the use of the polymyxin protocol varied based on provider discretion, thus creating the subgroups of infants who received either polymyxin or saline.

Outcomes and definitions

The primary outcome of PedVAE was previously defined by CDC National Healthcare Safety Network (NHSN)[5] as an increase in daily minimum mean airway pressure (MAP) or an increase in daily minimum (FiO_2) for 2 or more days following at least 2 days of stable or decreasing minimum MAP or FiO_2.

If a new antimicrobial agent was started during the ventilator-associated event (VAE) window period and the antibiotic was continued for ≥4 days, it was deemed a PedAVAE. A PedAVAE with a positive diagnostic test for infection was considered a probable ventilator-associated pneumonia (PVAP) case. Antibiotic days were determined based on dispensation data.

Unique growth of bacteria was defined as new growth of a species of pathogenic bacteria in a lower respiratory tract culture of an infant.

Data collection

Infants meeting the inclusion criteria were identified through our institution's data maintained in the Children's Hospitals Neonatal

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Table 1. Baseline Characteristics

Characteristic	Total (n=106)	Saline (n=52)	Polymyxin (n=54)	*P* Value
Sex, male, no. (%)	58 (55)	28 (54)	30 (56)	.86
Admission gestational age, median wk (IQR)	24 (23–25)	25 (24–26)	24 (23–25)	.055
Birth-to-admission interval, median d (IQR)	3.5 (0–14.5)	5.5 (1–18)	2.5 (0–9.75)	.042
Admission weight, median g (IQR)	740 (620–870)	810 (698–893)	655 (570–810)	.0009
Admission height, mean cm (SD)	31.6 (2.91)	32.2 (2.76)	31 (2.96)	.031
Black/African-American race, no. (%)	60 (56.6)	27 (51.9)	33 (61.1)	.34
White/Caucasian race, no. (%)	10 (9.4)	7 (13.5)	3 (5.6)	.098
Hispanic ethnicity, no. (%)	18 (17)	11 (21.2)	7 (13%)	.26

Note. SD, standard deviation; IQR, interquartile range.

Table 2. Ventilator-Associated Outcomes by Proportion and Incidence Rate

Variable	Total (n=106)	Saline (n=52)	Polymyxin (n=54)	Rate Ratio (95% CI)	*P* Value
PedVAE, no. (%)	19 (18)	5 (10)	14 (26)	. . .	. . .
PedVAE incidence rate per 1,000 ventilator days, PS adjusted comparison	6	4.7	5.8	1.24 (0.41–3.69)	.70
PedVAE incidence rate per 1,000 ventilator days, multiple events, PS adjusted comparison	6.3	4.7	6.1	1.32 (0.45–3.89)	.62
PedAVAE, no. (%)	11 (10)	4 (8)	7 (13)	. . .	. . .
PedAVAE incidence rate per 1,000 ventilator days, PS adjusted	3.7	3.8	3.4	0.9 (0.24–3.35)	.87
PVAP, no. (%)	5 (5)	2(4)	3 (5.6)	. . .	. . .
PVAP incidence rate per 1,000 ventilator days, PS adjusted comparison	1.7	1.7	1.7	0.98 (0.14–7.02)	.98

Note. PedVAE, pediatric ventilator-associated event; PedAVAE, pediatric antibiotic-related ventilator-associated event; PVAP, possible ventilator-associated pneumonia; PS, propensity score; CI, confidence interval. Adjustments for multiple events were made only where indicated.

Database (CHND). Clinical data were extracted through structured manual chart review using REDCap (Research Electronic Data Capture).[6]

Statistical analysis

Baseline characteristics and outcomes were summarized using mean and standard deviation for normally distributed continuous variables and median with interquartile range for nonnormally distributed data. Comparisons between groups were calculated using χ^2 test for categorical variables, unpaired *t* test for parametric continuous variables, and Wilcoxon rank-sum test for nonparametric continuous variables.

We used Poisson regression with propensity score adjustment for postmenstrual age on admission, admission weight, race, and birth-to-admission age to compare PedVAE rates. Little overlap of propensity scores was noted in the lowest propensity score decile; thus, analyses were repeated excluding infants in the lowest decile.

The PedVAE incidence rate was calculated as the total number of events as the numerator and total ventilator days contributed by each neonate included in the study population as the denominator, and this rate is reported as incidents per 1,000 ventilation days. PedVAE incidence rates and rate ratios were estimated using propensity score adjusted Poisson regression models.

Data analysis was performed using STATA version 15 software (StataCorp, College Station, TX) and SAS version 9.4 software (SAS Institute, Cary, NC). $P < .05$ was considered significant.

Results

Of the 136 infants identified, 30 were intubated for <3 days and were not included in the final analysis. Baseline characteristics are summarized in Table 1. The median number of polymyxin doses administered per infant was 18, with notable variation in total doses received (interquartile range [IQR], 6.3–55.8).

Infants in the polymyxin group were mechanically ventilated for a longer median duration of 38.5 days (IQR, 25.75–53.75) compared with 17 days (IQR, 9–33.5; $P = .009$) in the saline group during their qualifying admission. Mortality, length of stay, and antibiotic days were similar between groups (See Table 2).

In both the saline and polymyxin groups *Pseudomonas aeruginosa* and *Staphylococcus aureus* were the most commonly isolated bacterial species.

Discussion

This study is the first to evaluate the practice of polymyxin endotracheal suction catheter flushes in a high-risk cohort of intubated infants weighing <1,000 g. We found that polymyxin endotracheal

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suction catheter flushes did not lead to an observeable reduction in the CDC reportable outcome of PedVAE.

We observed a PedVAE rate of 6 per 1,000 ventilator days in our high-risk cohort. Corocos et al[7] reported a rate of ventilator-associated condition (VAC, using the same FiO_2 and MAP definitions as PedVAE) in a general NICU cohort to be ~3.1 per 1000 ventilator days, lower than our measure. The higher rate of PedVAE in our cohort could be due to inclusion of only extremely low birth-weight infants.[7] In total, 57% of PedVAEs were associated with antibiotic administration, a higher rate than previously reported in the NICU population (0%–43%).[8,9]

This study had several limitations inherent to a retrospective cohort design. The primary outcome of PedVAE can be the result of both infectious and noninfectious events. The outcomes of PedAVAE and PVAP may be more specific measures of the effect of polymyxin on ventilator-associated infection, but a larger sample size would be needed to detect a significant difference between groups. Provider discretion regarding which patient received polymyxin is a major limitation of our study because it may reflect the infants clinical status or risk assessment by the medical team, which is also suggested by the polymyxin group infants being smaller and younger than those in saline group. Despite statistical adjustment, influence of residual confounders needs to be considered while interpreting our results. Even after propensity score control we did find that PedVAE occurred more often in the group receiving polymyxin, which perhaps indicates a lack of benefit. Notable variation in the amount of polymyxin received by each infant interferes with drawing generalizable conclusions. The study sample was too small to make determinations about possible effects of polymyxin on mortality or length of stay. Subtherapeutic doses of antibiotics have been shown to lead to antibiotic resistance. Unfortunately, bacterial polymyxin resistance data were not available for our study cultures. Despite these limitations, our study provides baseline first data on the potential impact of antibiotic flushes in high-risk premature infants and will guide future study designs to investigate the knowledge gaps.

In conclusion, we report for the first time that PedVAE rates were not lower in infants who received polymyxin endotracheal catheter flushes in a tertiary NICU cohort of outborn premature infants weighing <1,000 g. The incidence rate of PedVAE in this high-risk extremely low birth-weight neonatal cohort was 6 per 1,000 ventilator days, higher than the previously reported incidence in a general NICU population.

Supplementary material. To view supplementary material for this article, please visit https://doi.org/10.1017/ice.2022.253

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