Hospital Associated and Ventilator Acquired Bacterial Pneumonia in Infants and Children

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Introduction

- The incidence of hospital acquired and ventilator associated pneumonias (HABP/VABP) in infants and children is unclear.
- Risk factors predisposing children and infants to HABP/VABP are poorly understood.
- Enrollment in clinical trials of novel antibiotics for HABP/VABP could be improved through a better understanding and identification of infants and children at risk for HABP/VABP.

Methods

- We prospectively identified and enrolled children admitted to an intermediate or intensive care unit at 9 children's hospitals in this observational study.
- Inclusion criteria:
  - Hospitalized for ≥48 hours or readmitted <7 days after discharge
  - <120 days old: ≥5 days mechanical ventilation
  - ≥ 120 days to 18 years: >24 hours of: high flow oxygen, BiPAP, CPAP or mechanical ventilation
- We evaluated medical records daily for HABP/VABP until discharge from unit or until meeting HABP/VABP definition.
- FDA-defined HABP/VABP (≥1 of each below):
  - Chest x-ray with a new or progressive infiltrate suggestive of bacterial pneumonia.
  - New or worsening cough, dyspnea, tachypnea or new sputum production, or hypoxemia, or new need for mechanical ventilator, or need for acute changes in ventilator settings or new suctioned respiratory secretions.
  - Systemic inflammation: fever, hypothermia, leukocytosis, leukopenia, >15% immature neutrophils or C-reactive protein >5 mg/dL.
  - Timing: signs/symptoms of pneumonia first developed >48 hours after admission or >48 hours after initiation of mechanical ventilation.
- We defined eligibility for clinical trial enrollment as receiving <48 hours of antibiotics prior to meeting the definition for HABP/VABP.
- Statistics:
  - Overall and for infants <120 and ≥120 days old, we calculated the cumulative incidence of HABP/VABP.
  - We used Fisher's exact and Wilcoxon rank-sum tests to compare risk factor exposures for children with and without HABP/VABP.
  - Using a backwards-selection stepwise regression, we identified risk factors associated with HABP/VABP in the high-risk population overall, for infants <120 days and ≥120 days old.
  - For enrolled patients who were treated with antibiotics, we calculated the proportion that would have been eligible for a clinical trial of an antibiotic for HABP/VABP.

Results

- 800 children were enrolled.
- The median age was 1.3 years (interquartile range; 0.3, 7.2).
- HABP/VABP was diagnosed in 10% (82/800) overall, 10% (21/206) of infants <120 days old and 10% (61/594) of infant ≥ 120 days old.
- The duration of mechanical ventilation was longer and the use of inotropes, corticosteroids, and acid suppressing agents were more frequent in children who developed HABP/VABP (Table 1).
- On multivariable analysis, risk factors varied by age (Tables 2-4).
- Overall, 43% (103/238) of children receiving respiratory support who were started on an antibiotic would have met FDA-criteria for inclusion in a clinical trial for HABP/VABP: 35% (34/96) of those <120 days of age and 49% (69/142) of those ≥ 120 days of age.

Table 1. Treatment exposures and medications

	HABP/VABP N=82	No HABP/VABP N=718	P
Ventilation			
Invasive mechanical ventilation	90%	88%	0.59
Duration of invasive mechanical ventilation (days)	14 (6, 28)	7 (4, 14)	<0.01
Noninvasive mechanical ventilation (CPAP or BiPAP)	32%	44%	0.03
Duration of noninvasive mechanical ventilation (days)	3 (1, 6)	3 (1, 7)	0.44
Enteral nutrition			
Nasogastric tube	46%	44%	0.82
Naso-duodenal/-jejunal tube	20%	24%	0.49
Percutaneous (PEG, GJ, J-tube)	42%	31%	0.06
Medications			
Inotropic therapy	38%	51%	0.03
Chemotherapy at current hospitalization	2%	3%	>0.99
Chemotherapy in past 60 days	5%	4%	0.77
Biologic agents at hospital admission	2%	2%	>0.99
Biologic agents in past 6 months	2%	1%	0.23
Corticosteroids at current hospitalization	17%	13%	0.31
Corticosteroids in past 60 days	7%	2%	0.01
Acid suppressing therapy	48%	63%	0.01
Blood transfusion in prior 7 days	30%	24%	0.35
Systemic antibacterials within 90 days	83%	85%	0.52
Other			
Frequent suctioning	64%	34%	<0.01
Mechanical circulatory support	4%	5%	0.79
Massive volume resuscitation	11%	13%	0.61
Invasive monitoring	34%	35%	>0.99

Values are median (interquartile range) for continuous variables and % for categorical variables

Table 2. Factors associated with HABP/VABP for patients < 18 years old.

	OR (95% confidence interval)
Age (years)	1.31 (1.12, 1.54)
Height (cm)	0.95 (0.93, 0.98)
ICU length of stay at enrollment (days)	1.01 (1.00, 1.02)
Aspiration risk	3.69 (1.79, 7.60)
Noninvasive ventilation	0.59 (0.30, 1.18)
Inotropic therapy	0.59, 0.30, 1.18)
Biologic agents at hospital admission	4.62 (0.86, 24.79)
Acid suppressing therapy	0.57 (0.29, 1.14)
Blood transfusion in prior 7 days	3.84 (1.87, 7.88)
Frequent suctioning	4.46 (2.19, 9.09)
Massive volume resuscitation	0.37 (0.10, 1.41)

Table 3. Factors associated with HABP/VABP for patients ≥ 120 days old.

	OR (95% confidence interval)
Age (yr)	1.20 (1.00, 1.44)
Height (cm)	0.97 (0.94, 1.00)
ICU length of stay at enrollment (days)	1.01 (1.00, 1.02)
Aspiration risk	4.86 (2.10, 11.24)
Biologic agents at hospital admission	7.73 (1.36, 44.09)
Blood transfusion in prior 7 days	3.41 (1.42, 8.23)
Frequent suctioning	8.73 (3.03, 25.21)
Massive volume resuscitation	0.34 (0.07, 1.66)

Table 4. Factors associated with HABP/VABP for patients < 120 days old.

	OR (95% confidence interval)
Weight (kg)	0.33 (0.18, 0.61)
ICU length of stay at enrollment (days)	1.03 (1.00, 1.05)
Noninvasive ventilation	0.36 (0.11, 1.22)
Acid suppressing therapy	0.31 (0.08, 1.21)
Blood transfusion in prior 7 days	4.13 (1.20, 14.25)
Frequent suctioning	5.25 (1.35, 20.45)

Conclusions

- Systematic prospective observation identified HABP/VABP in 10% of infants and children receiving respiratory support.
- Additional risk factors associated with HABP/VABP differed by age.
- 43% of pediatric patients needing antibiotics and receiving respiratory support could be eligible for an antibiotic clinical trial.

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