Endotracheal Intubation in Neonates: A Prospective Study of Adverse Safety Events in 162 Infants

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Objective To determine the rate of adverse events associated with endotracheal intubation in newborns and modifiable factors contributing to these events.

Study design We conducted a prospective, observational study in a 100-bed, academic, level IV neonatal intensive care unit from September 2013 through June 2014. We collected data on intubations using standardized data collection instruments with validation by medical record review. Intubations in the delivery or operating rooms were excluded. The primary outcome was an intubation with any adverse event. Adverse events were defined and tracked prospectively as nonsevere or severe. We measured clinical variables including number of attempts to successful intubation and intubation urgency (elective, urgent, or emergent). We used logistic regression models to estimate the association of these variables with adverse events.

Results During the study period, 304 intubations occurred in 178 infants. Data were available for 273 intubations (90%) in 162 patients. Adverse events occurred in 107 (39%) intubations with nonsevere and severe events in 96 (35%) and 24 (8.8%) intubations, respectively. Increasing number of intubation attempts (OR 2.1, 95% CI, 1.6-2.6) and emergent intubations (OR 4.7, 95% CI, 1.7-13) were predictors of adverse events. The primary cause of emergent intubations was unplanned extubation (62%).

Conclusions Adverse events are common in the neonatal intensive care unit, occurring in 4 of 10 intubations. The odds of an adverse event doubled with increasing number of attempts and quadrupled in the emergent setting. Quality improvement efforts to address these factors are needed to improve patient safety. *(J Pediatr 2016;168:62-6)*.

Infants in the neonatal intensive care unit (NICU) are among the highest risk groups for adverse events in the hospital setting.[1,2] In adult intensive care units and pediatric intensive care units (PICUs), adverse events related to endotracheal or tracheostomy tubes comprise a substantial proportion of total adverse events and lead to significant patient harm.[3-6] Little is documented about airway safety in the NICU.

In PICUs, 19%-41% of all endotracheal intubation procedures are associated with adverse events.[7-10] Studies from the National Emergency Airway Registry for Children (NEAR4Kids) report that in children beyond the newborn period, these adverse events are associated with patient,[9] provider,[10] and practice factors.[11] Studies of endotracheal intubation in the NICU have focused primarily on proficiency, mainly of trainees, and use of premedications.[12-17] Few studies have reported rates and types of adverse events associated with endotracheal intubation in critically ill newborns and potentially modifiable factors associated with these complications.[18] As a result, evidence-based interventions to improve airway safety in this vulnerable population are lacking. We hypothesized that in critically ill newborns in the NICU, adverse events associated with intubation would match or exceed the rate in children or adults. Our objectives were to describe the rate and types of adverse events associated with endotracheal intubation in the NICU and identify potentially modifiable factors associated with these events.

Methods

We conducted a prospective, observational study in the 100-bed, academic, level IV (regional) NICU of the Vanderbilt University Medical Center. Endotracheal intubations are performed by pediatric residents, neonatal

NEAR4Kids	National Emergency Airway Registry for Children
NICU	Neonatal intensive care unit
PICU	Pediatric intensive care unit

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nurse practitioners/hospitalists, neonatologists, anesthesiologists, and otolaryngologists. Premedication for intubation was commonly used and consisted of an opiate and a benzodiazepine, though no formal protocol existed at the time of this study. The Vanderbilt Institutional Review Board approved the study with waiver of consent for infants and providers.

All intubations that occurred in the NICU from September 1, 2013, through June 30, 2014, were eligible for inclusion. To ensure high quality data collection, we excluded intubations that occurred in areas outside of the NICU such as the delivery room, operating room, or during transport. Study personnel completed daily medical record review of all infants in the NICU to determine eligible intubations.

We developed 2 standardized data collection tools. Our primary tool was a voluntary Post-Intubation Provider Survey that the intubating clinician completed after an intubation encounter and that documented the presence of any of the a priori defined adverse events (**Appendix 1**; available at www.jpeds.com). Our secondary tool was an Intubation Procedural Record that the bedside nurse completed during the intubation. The study principal investigator (L.H.) also validated 3 adverse events (chest compressions, hypotension receiving treatment, mainstem bronchial intubation) through standardized medical record review. We defined intubation encounters, courses, and attempts as described by Nishisaki et al[9] for the NEAR4Kids investigators. Briefly, an encounter was defined as 1 completed episode of airway management and could involve multiple courses. Courses were one approach (oral, nasal, or bronchoscopy) to secure an airway and could include multiple attempts. An attempt began when the laryngoscope entered the mouth and ended with laryngoscope removal.

Study Outcomes

The primary safety outcome of our study was an intubation encounter with 1 or more adverse events. We defined these adverse events (**Table I**) a priori based on literature review and local expert opinion. We used strict operational definitions for each adverse event to minimize bias (**Appendix 2**; available at www.jpeds.com). To allow comparison with available pediatric data,[9] we classified these events as either nonsevere or severe. Secondary outcomes were severe hypoxemia (oxygen saturation <60%) and bradycardia (heart rate less than 60 beats per minute for 5 seconds) during the intubation encounter. We tracked these serious events as a measure of infant stability during intubation, although to allow comparison with available pediatric data, they were not classified as adverse events and were not included in our primary analyses.[8-11,18]

Independent Variables

We measured clinical variables that have either been associated with adverse events in older patients or which we hypothesized would be pertinent in neonates. Intubations were defined as elective, urgent, or emergent. Intubations were defined as urgent when an artificial airway was needed imminently (within 4 hours), but time was available for premedication and preprocedural patient stabilization. An intubation was classified as emergent if establishment of an airway was considered immediately necessary because of vital sign instability and time was not available for premedications or effective bag-mask ventilation/preoxygenation could not be sustained. All other intubations were classified as elective.

Statistical Analyses

We used both univariable and multivariable logistic regression models to examine the associations between clinical variables and adverse events. Our multivariable model included 4 variables that we hypothesized a priori would be associated with adverse events: postmenstrual age, premedication use, first-attempt proceduralists' clinical role, and intubation urgency. Generalized estimating equations were used to fit marginal logistic regression models with clustering within patients to account for multiple intubation encounters per patient.[19] Our primary analysis included only intubations with a completed Post-Intubation Provider Survey. To test the implications of missing data, we performed sensitivity analyses by coding all excluded intubations as either having an adverse event or not having an adverse event. We then re-estimated each logistic regression model to evaluate if our OR estimates changed enough to alter our final conclusions. To attempt to estimate under- or overreporting of

Table I. Intubation associated adverse events by severity (n = 273 neonatal intubation encounters)

Nonsevere events, n (%)		Severe events, n (%)	
Any	96 (35)	Any	24 (8.8)
Esophageal intubation with immediate recognition	58 (21.4)	Hypotension receiving treatment*	10 (3.7)
Oral/airway bleeding	26 (9.5)	Transition to emergent	9 (3.3)
Difficult bag-mask ventilation	20 (7.3)	Chest compressions†	8 (2.9)
Mainstem bronchial intubation (confirmed by chest radiograph)	19 (7)	Code medications	2 (0.7)
Emesis	6 (2.2)	Pneumothorax	1 (0.4)
Chest wall rigidity‡	3 (1.1)	Direct airway trauma	1 (0.4)
		Death	1 (0.4)
		Esophageal intubation with delayed recognition	0

*Two infants were receiving treatment for hypotension prior to intubation but had escalation of treatment after intubation.
†Four infants were receiving chest compressions at the time of the first intubation attempt that continued during the intubation attempts.
‡Two of 3 infants were treated with emergent intubation. No infant received pharmacologic treatment for chest wall rigidity.