



Published in final edited form as:

J Perinatol. 2016 February ; 36(2): 112–115. doi:10.1038/jp.2015.158.

Failed Endotracheal Intubation and Adverse Outcomes Among Extremely Low Birth Weight Infants

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Abstract

OBJECTIVE—To quantify the importance of successful endotracheal intubation on the first attempt among extremely low birth weight (ELBW) infants who require resuscitation after delivery.

STUDY DESIGN—A retrospective chart review was conducted for all ELBW infants < 1000 g born between January 2007 and May 2014 at a level IV neonatal intensive care unit. Infants were included if intubation was attempted during the first five minutes of life, or if intubation was attempted during the first 10 minutes of life with heart rate < 100. The primary outcome was death or neurodevelopmental impairment. The association between successful intubation on the first attempt and the primary outcome was assessed using multivariable logistic regression with adjustment for birth weight, gestational age, gender, and antenatal steroids.

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There are no prior publications or submissions with any overlapping information. This manuscript is being submitted only to the *Journal of Perinatology*, and it will not be submitted elsewhere while under consideration. No external funding was secured for this study. The authors have no financial relationships relevant to this article to disclose. The authors have no conflicts of interest to disclose. All authors meet the stated author requirements and are responsible for reported research, and have contributed to this case and manuscript. All authors have approved the final manuscript as submitted and take full responsibility for the manuscript. Matthew Wallenstein wrote the first draft of the manuscript.

Contributors' Statements

Matthew B. Wallenstein conceptualized and designed the study, drafted the initial manuscript, and approved the final manuscript as submitted.

Yassar Arain assisted with data collection, reviewed and revised the manuscript, and approved the final manuscript as submitted.

Krista L. Birnie assisted with data collection, reviewed and revised the manuscript, and approved the final manuscript as submitted.

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David K. Stevenson designed the study, reviewed and revised the manuscript, and approved the final manuscript as submitted.

RESULTS—The study sample included 88 ELBW infants. Forty-percent were intubated on the first attempt and 60% required multiple intubation attempts. Death or neurodevelopmental impairment occurred in 29% of infants intubated on the first attempt, compared to 53% of infants that required multiple attempts, adjusted odds ratio 0.4 (95% confidence interval 0.1 - 1.0), $p < 0.05$.

CONCLUSION—Successful intubation on the first attempt is associated with improved neurodevelopmental outcomes among ELBW infants. This study confirms the importance of rapid establishment of a stable airway in ELBW infants requiring resuscitation after birth and has implications for personnel selection and role assignment in the delivery room.

Keywords

Extremely low birth weight; endotracheal intubation; neurodevelopmental impairment; resuscitation; failed intubation; intubation attempt

INTRODUCTION

Endotracheal intubation can be a lifesaving procedure for newborn infants with inadequate ventilation after birth.¹⁻² The process of intubation itself is associated with adverse physiologic changes, including increased intracranial pressure and rapid deterioration of heart rate and oxygen saturation.³⁻⁸ Failed or prolonged intubation attempts lead to persistence of these physiologic changes and persistence of inadequate ventilation and oxygenation.

Rapid and effective intubation is ideal. However, in a recent study of delivery room resuscitation, only 30% of infants were successfully intubated on the first attempt and 40% required three or more attempts,⁹ primarily due to failed attempts by inexperienced trainees.^{3, 9-10}

Extremely low birth weight (ELBW) infants who receive cardiopulmonary resuscitation have increased risk of mortality and neurological injury.¹¹⁻¹³ However, extensive resuscitative measures often occur prior to establishing adequate ventilation.¹⁴ We hypothesize that rapid intubation may obviate the need for cardiopulmonary resuscitation and, in turn, improve neonatal morbidity and mortality.

Our objective was to investigate whether intubation on the first attempt compared to failed first attempt was associated with less death or neurodevelopmental impairment among ELBW infants who required resuscitation after delivery.

METHODS

A retrospective chart review was conducted for all ELBW infants < 1000 g born at Lucile Packard Children's Hospital at Stanford between January 2007 and May 2014. This study population was a convenience sample of available electronic data from our institution. This study was approved by our institutional review board, and all research components adhered to institutional ethical human research guidelines.

Medical record numbers were identified using the Stanford Translational Research Integrated Database Environment (STRIDE) with the following search criteria: (1) birth weight \geq 1000 g, and (2) date of birth within the study period.¹⁵ Chart reviews were conducted for all infants identified by STRIDE. Infants were included in the final analysis if intubation was attempted during the first five minutes of life, or if intubation was attempted during the first 10 minutes of life with heart rate $<$ 100. These inclusion criteria were developed to identify unstable ELBW infants requiring resuscitation after birth—a group that may benefit from rapid establishment of effective ventilation. Intubation attempt was defined as insertion of laryngoscope blade into the airway. There is no standard policy at our institution for routine intubation of ELBW infants in the delivery room. Intubation was performed at the discretion of the individual provider and was based on the clinical status of the infant. Surfactant is not administered in the delivery room at our institution.

Infants were excluded if birth occurred at an outside hospital, if delivery record details were insufficient to establish number of intubation attempts, or if long-term follow-up data were unavailable.

Demographic, maternal, and postnatal information was collected. Number of attempts until successful intubation was recorded. Infants intubated on the first attempt were compared to infants who required multiple intubation attempts. The primary outcome was a composite of death or neurodevelopmental impairment at 18-22 months of age, which was defined as any one of the following: cognitive composite score \leq 70 on the Bayley Scales of Infant and Toddler Development, third edition (BSID-III),¹⁶ moderate or severe cerebral palsy, severe hearing impairment, or bilateral visual impairment. Cerebral palsy was defined as non-progressive abnormality of muscle tone in one or more extremities.¹⁷ Hearing impairment was defined as severe impairment indicated by formal audiology evaluation. Visual impairment was defined as vision worse than 20/200. Similar criteria for neurodevelopmental impairment have been used in prior studies of ELBW infants.¹⁸ Scores from the Capute Scales (a norm-referenced developmental assessment tool that is highly correlated with the Bayley Scales) were used if BSID-III scores were not available, with neurodevelopmental impairment defined by adjusted full scale Capute developmental quotient (DQ) \leq 70. The Capute full scale DQ is a composite of the Cognitive Adaptive Test for visual-motor development and the Clinical Linguistic and Auditory Scale for language development.

Delivery room outcomes included 5 minute Apgar score, chest compressions initiated after first intubation attempt, and use of epinephrine (either intravenous or endotracheal). Neonatal outcomes included severe intraventricular hemorrhage (IVH, grade 3 or 4), bronchopulmonary dysplasia (BPD), periventricular leukomalacia (PVL), necrotizing enterocolitis (NEC, Bell stage II or greater), severe retinopathy of prematurity (ROP), pneumothorax, and patent ductus arteriosus (PDA). BPD was defined as use of supplemental oxygen at 36 weeks postmenstrual age. Severe ROP was defined as threshold retinopathy or the need for ophthalmologic intervention.¹⁹

Statistical analysis was performed using Statistical Analysis Software, version 4.1 (SAS Institute Inc, Cary, NC, 2003). Measures of central tendency were used to describe data,

including mean, standard deviation, median, and interquartile range for continuous variables. Binary and categorical variables were described using frequencies and percentages. Infants successfully intubated on the first attempt were compared to infants who required multiple attempts using student's t test, the chi squared test, Fisher's exact test, and the Wald test as appropriate. Multivariable logistic regression was used to adjust for potential confounding variables, including birth weight, gestational age, sex, and antenatal steroid administration. Statistical significance was set as a p value of < 0.05 .

RESULTS

During the study period, 378 ELBW infants were treated at our institution, of whom 88 met study inclusion criteria. Among these 88 infants who required intubation within five minutes of life or within 10 minutes of life if heart rate < 100 , 40% were intubated on the first attempt, 34% on the second attempt, and 26% required three or more attempts. Infants intubated on the first attempt were more likely to be female ($p < 0.05$). Other demographic and baseline characteristics were no different between the two groups (Table 1).

Results of delivery room, neonatal, and neurodevelopmental outcomes are shown in Tables 2-4. Death or neurodevelopmental impairment occurred in 29% of infants intubated on the first attempt, compared to 53% of infants that required multiple attempts with adjusted odds ratio (aOR) 0.4, 95% confidence interval (CI) 0.1 - 1.0, $p < 0.05$.

Estimated risks for the additional study outcomes were less statistically stable, but there were non-significant trends towards reduced risk of adverse delivery room and neonatal outcomes among infants intubated on the first attempt, including chest compressions after intubation attempt (aOR 0.4, 95% CI 0.1-1.4), use of epinephrine (aOR 0.4, 95% CI 0.1-2.4), IVH (aOR 0.4, 95% CI 0.1-1.4), PVL (aOR 0.2, 95% CI 0.02-1.5), NEC (aOR 0.2, 95% CI 0.05-1.2), and pneumothorax (aOR 0.5, 95% CI 0.1-2.7).

Given the differential success of first intubation by sex, we performed an additional analysis of the primary outcome stratified by sex and did not find a significant difference in risk reduction between males and females who were intubated on the first attempt.

DISCUSSION

Among ELBW infants who required resuscitation at birth, successful intubation on the first attempt was associated with reduced risk of death or neurodevelopmental impairment compared with infants requiring multiple intubation attempts. Our results emphasize the importance of rapid establishment of a stable airway in ELBW infants requiring resuscitation in the delivery room, which is consistent with prior studies.³

Our stringent inclusion criteria selected for the most critically ill ELBW infants at birth—a group that has been shown to have an increased risk of morbidity and mortality compared to other ELBW cohorts.¹¹⁻¹³ However, the frequency of adverse outcomes was low among infants who were intubated on the first attempt. Likewise, higher frequencies of adverse outcomes were associated with failed intubation. For example, almost 1/3 of infants who required multiple intubation attempts also received chest compressions or epinephrine in the

delivery room. Based on these results, it appears that rapid establishment of an effective airway may mitigate some of the risks associated with extensive resuscitation, especially if the primary cause of clinical instability is ineffective oxygenation and ventilation.

On the other hand, it is possible that ELBW infants who are predisposed to death or neurodevelopmental impairment are also more difficult to intubate at birth. This explanation seems unlikely, given similar baseline characteristics between the two groups of infants, with the exception of sex, and no biologically plausible mechanism.

In addition to neurodevelopmental outcomes, successful intubation was also associated with non-significant trends towards reduced risks of adverse delivery room and neonatal outcomes, including cardiopulmonary resuscitation, severe IVH, PVL, NEC, and pneumothorax. The adverse physiologic changes associated with failed intubation, such as increased intracranial pressure or prolonged hypoxia, may contribute to these outcomes, which themselves may contribute to long-term neurodevelopmental impairment among infants requiring multiple intubation attempts.

We observed that male infants were less likely to be intubated on the first attempt. Analysis of the primary outcomes stratified by sex suggests that patient sex alone did not account for the risk reduction between infants intubated on the first attempt and those who were not. The lower likelihood of successful intubation among males may be due to chance, but there is some evidence that male sex is associated with poorer laryngoscopic view in children,²⁰ and that male infants require more extensive resuscitation than female infants.²¹ Difficulty with airway management among males may contribute to overall sex differences in long-term outcomes among ELBW infants.²² However, the present study was not designed to answer this question.

Our results lead us to speculate that airway management of ELBW infants in the delivery room should be reserved for experienced practitioners. Endotracheal intubation of ELBW infants by resident trainees, whose success rates are as low as 20%,²³ should be limited to controlled settings in the neonatal intensive care unit (NICU) where effective bag-mask ventilation has already been established. Efforts to provide adequate intubation experience to residents, which is lacking at many institutions,¹⁰ should focus on simulation training or more stable patient populations.

There are several major limitations of the present study. First, our sample size was small and not sufficiently powered to detect differences in secondary outcomes. Second, the generalizability of our results is unclear, given that our study population was derived from a single tertiary NICU. Third, more detailed resuscitation information, including training level of the initial intubator and specific reason for initial intubation, was not available.

CONCLUSION

We found that successful intubation on the first attempt is associated with improved neurodevelopmental outcomes among ELBW infants, which has implications for personnel selection and role assignment during delivery room resuscitation. These results should be replicated in larger populations.

Abbreviations

ELBW	Extremely low birth weight
STRIDE	Stanford Translational Research Integrated Database Environment
BSID-III	Bayley Scales of Infant and Toddler Development, third edition
DQ	developmental quotient
IVH	intraventricular hemorrhage
BPD	bronchopulmonary dysplasia
PVL	periventricular leukomalacia
NEC	necrotizing enterocolitis
ROP	retinopathy of prematurity
PDA	patent ductus arteriosus
aOR	adjusted odds ratio
CI	confidence interval
NICU	neonatal intensive care unit

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Table 1

Demographic, Maternal, and Baseline Delivery Room Characteristics

Variables	Successful Intubation on First Attempt (n= 35)	Failed Intubation on First Attempt (n= 53)	P Value
Gestational age (weeks)	26.4 ± 1.4	26.0 ± 1.6	0.27
Birth weight (grams)	771 ± 143	758 ± 146	0.68
Sex (female)	22 (62.9)	20 (37.7)	0.02
Maternal Race			0.72
African-American	1 (2.9)	2 (3.8)	
Caucasian	7 (20.0)	7 (13.2)	
Latino	13 (37.1)	21 (39.6)	
Asian	10 (28.6)	12 (22.6)	
Other	4 (11.4)	11 (20.8)	
Antenatal steroids (completed course)	20 (57.1)	35 (66.0)	0.40
Cesarean delivery	27 (77.1)	40 (75.5)	0.86
Apgar 1 minute	2 (2)	2 (3)	0.76
Chest compressions performed prior to first intubation attempt	5 (14.3)	4 (7.5)	0.47

Data reflect mean ± standard deviation or n (%) or median (interquartile range), T-test for continuous variables (gestational age and birth weight), Wilcoxon Rank Sum test for Apgar 1 minute, Chi-square test for categorical variables, and Fisher exact test for chest compressions.

Table 2

Delivery Room Outcomes

Outcomes	Successful Intubation on First Attempt (n= 35)	Failed Intubation on First Attempt (n= 53)	Crude OR (95% CI) or <i>p</i> value	aOR (95% CI) or <i>p</i> value*
Apgar 5 minutes	6 (3)	5 (4)	0.14	---
Chest compressions performed after first intubation attempt	5 (14.3)	15 (28.3)	0.4 (0.1-1.3)	0.4 (0.1-1.4)
Epinephrine	2 (5.7)	8 (15.1)	0.3 (0.1-1.7)	0.4 (0.1-2.4)

Data reflect median (interquartile range) or n (%), Wilcoxon Rank Sum test for Apgar 5 minute and -Wald test for binary outcomes

* Adjusted for birth weight, gestational age, gender, and antenatal steroids

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Table 3

Neonatal Outcomes

Outcomes	Successful Intubation on First Attempt (n= 35)	Failed Intubation on First Attempt (n= 53)	Crude OR (95% CI)	aOR (95% CI) *
IVH, grade 3 or 4	5 (14.3)	14 (26.4)	0.4 (0.1-1.4)	0.4 (0.1-1.4)
ROP	6 (17.1)	6 (11.3)	1.4 (0.4-4.9)	1.6 (0.4-6.8)
BPD	17 (48.6)	25 (47.2)	0.7 (0.3-1.9)	0.9 (0.3-2.5)
PVL	1 (2.9)	8 (15.1)	0.2 (0.02-1.4)	0.2 (0.02-1.5)
NEC, stage 2 or greater	2 (5.7)	10 (18.9)	0.3 (0.1-1.3)	0.2 (0.05-1.2)
Pneumothorax	2 (5.7)	6 (11.3)	0.4 (0.1-2.3)	0.5 (0.1-2.7)
PDA	20 (57.1)	24 (45.3)	1.4 (0.6-3.3)	1.3 (0.5-3.2)

Data reflect n (%), Wald test for all outcomes

* Adjusted for birth weight, gestational age, gender, and antenatal steroids

Table 4

Mortality and Neurodevelopmental Outcomes

Outcomes	Successful Intubation on First Attempt (n= 35)	Failed Intubation on First Attempt (n= 53)	Crude OR (95% CI)	aOR (95% CI) **
Death or neurodevelopmental impairment *	10 (28.6)	28 (52.8)	0.4 (0.1-0.9)	0.4 (0.1-1.0)
Death	4 (11.4)	13 (24.5)	0.4 (0.1-1.3)	0.4 (0.1-1.7)
Neurodevelopmental impairment *	6 (17.1)	15 (28.3)	0.4 (0.1-1.2)	0.4 (0.1-1.3)

Data reflect n (%), Wald test for all outcomes

* Any one of the following: BSID-III score < 70, Capute full-scale DQ < 70, cerebral palsy, hearing impairment, bilateral visual impairment.

** Adjusted for birth weight, gestational age, gender, and antenatal steroids