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Neonatal Morbidities among Moderately Preterm Infants with and without Exposure to Antenatal Corticosteroids

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All authors approved the final manuscript as submitted and agree to be accountable for all aspects of the work.

Conflict of Interest

None.

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Abstract

Objective—We aimed to compare the rates of “surfactant treated respiratory disease” and other neonatal morbidities among moderately preterm (MPT) infants exposed to no, partial, or a complete course of antenatal corticosteroids (ANS).

Study Design—This observational cohort study evaluated MPT infants (29^{0/7}–33^{6/7} weeks' gestational age), born between January 2012 and November 2013 and enrolled in the “MPT Registry” of the National Institute of Child Health and Human Development Neonatal Research Network.

Results—Data were available for 5,886 infants, including 676 with no exposure, 1225 with partial, and 3,985 with a complete course of ANS. Among no, partial, and complete ANS groups, respectively, there were significant differences in rates of delivery room resuscitation (4.1, 1.4, and 1.2%), surfactant-treated respiratory disease (26.5, 26.3, and 20%), and severe intracranial hemorrhage (3, 2, and 0.8%). Complete ANS course was associated with lower surfactant-treated respiratory disease, compared with partial ANS (odds ratio [OR] 0.62; 95% confidence interval [CI] 0.52–0.74), and no ANS groups (OR 0.52; 95% CI 0.41–0.66) on adjusted analysis.

Conclusion—In MPT infants, ANS exposure is associated with lower delivery room resuscitation, surfactant-treated respiratory disease, and severe intracranial hemorrhage; with the lowest frequency of morbidities associated with a complete course.

Keywords

antenatal steroids; surfactant; gestational age; intracranial hemorrhage; necrotizing enterocolitis

Moderately preterm (MPT) neonates (born between 29^{0/7} and 33^{6/7} weeks' gestational age [GA]) represented approximately 2% of all births and 20% of all preterm births in the United States in 2014, and remain a relatively understudied group of high-risk infants.¹ MPT infants are at higher risk of adverse neonatal morbidities and long-term behavioral problems and disabilities including cerebral palsy, learning difficulties, and autism, compared with infants born at 37 weeks' GA or later.^{2–6}

The National Institute of Health consensus conference in 1994 supported the administration of antenatal corticosteroids (ANS) to women who are likely to deliver prior to 34 weeks' GA.⁷ ANS administration has been noted to improve survival and to reduce rates of respiratory distress syndrome (RDS), necrotizing enterocolitis (NEC), and intra-cranial hemorrhage (ICH) among preterm neonates.^{8–10}

Previous studies have evaluated outcomes of collective cohorts of extremely preterm neonates as well as MPT neonates ranging from 24 to 34 weeks' GA.^{9,11,12} At present, there is a scarcity of data on morbidities among MPT neonates born after exposure to a complete or a partial course of ANS in comparison to those born without any ANS exposure. Despite

recommendation for administration of ANS to women at risk of preterm delivery (< 34 weeks' GA), there is limited evidence to guide ANS use among women at risk of delivering MPT infants. As the risk of mortality and morbidities among MPT infants is different from infants born at extreme prematurity, benefits and risks associated with exposure to ANS among MPT infants may be different from those noted in extreme premature infants.

The primary aim of the current study was to compare the rates of surfactant-treated respiratory disease and other neonatal morbidities among a cohort of recently born MPT neonates exposed to no, partial, and a complete course of ANS. The secondary aims were to evaluate the risk factors associated with surfactant-treated respiratory disease in MPT infants, and to evaluate the association between no, partial, or complete ANS and neonatal morbidities at GAs from 29 to 33 weeks.

Methods

Study Design

This study is a retrospective analysis of prospectively collected data in a cohort of MPT infants born between January 2012 and November 2013 who were part of the Moderate Preterm Registry of the *Eunice Kennedy Shriver* National Institute of Child Health and Human Development (NICHD) Neonatal Research Network (NRN).¹³ The Moderate Preterm Registry included infants born at GA 29^{0/7} to 33^{6/7} weeks and admitted prior to 72 hours of age at NRN centers.¹³ All participating sites obtained approval from their Institutional Review Board prior to data collection. All sites, except three, received waiver of consent for collection of data.

Study Population

All neonates born at GA 29^{0/7} to 33^{6/7} weeks and enrolled in the Moderate Preterm Registry were included. Outborn infants and infants with major congenital anomalies were excluded from the analysis. Patients were classified into three groups: no ANS, partial ANS (1 dose of betamethasone, or < 4 doses of dexamethasone), and complete course of ANS (2 doses of betamethasone, or 4 doses of dexamethasone).

Maternal data including race, marital status, medical insurance, maternal hypertension, clinical chorioamnionitis, histologic chorioamnionitis (based on placental pathology), prolonged rupture of membranes (> 18 hours), mode of delivery, multiple births, and ANS administration were collected. Maternal hypertension was defined as either systolic blood pressure above 140 mm Hg or diastolic blood pressure above 90 mm Hg on at least two occasions, either before or during pregnancy. Major congenital anomalies were defined as either the anomalies that were incompatible with life or incompatible with life without drastic surgical or other measures.

Neonatal data were collected from birth until death, discharge, or 40 weeks' postmenstrual age, whichever occurred first, and included GA in completed weeks and days, birth weight, gender, resuscitation in the delivery room (DR), Apgar score, severity of ICH, presence of cystic periventricular leukomalacia (cPVL), endotracheal intubation, surfactant administration, respiratory support at 28 days of life, sepsis, dates of first oral feeding and

full oral feedings, and NEC. Patent ductus arteriosus (PDA) was defined as clinical evidence of PDA or confirmed by an echocardiogram.

We evaluated advanced level of resuscitation in the DR, defined as receipt of chest compression, and/or epinephrine. Severe ICH was defined as grade 3 or 4 ICH based on the head ultrasound (HUS) with the most severe grade of hemorrhage within first 28 days of age recorded.¹⁴ cPVL was defined as the presence of cystic echolucencies in the periventricular white matter on HUS closest to 28 days or closest to 36 weeks. NEC was defined by modified Bell's stage IIA.¹⁵ Small for gestational age (SGA) was defined as birth weight less than the tenth percentile based on the Alexander growth curve.¹⁶ Early and late-onset sepsis was defined by positive blood cultures taken before or after 72 hours of postnatal age, respectively.

Outcomes

The primary outcome was surfactant-treated respiratory disease.

Secondary outcomes were resuscitation and endotracheal intubation in the DR, in-hospital mortality, severe ICH, oxygen use at 28 days, and length of hospital stay.

Statistical Analysis

Distributions and proportions of baseline demographic characteristics and clinical outcomes were tabulated for the no ANS, partial ANS, and complete ANS groups. Continuous variables were expressed as mean values $\pm$ standard deviation and categorical variables as counts and percentages. Baseline characteristics and outcomes were compared among the three groups using chi square test, *t*-test, and analysis of variance as appropriate.

Multiple logistic regression or general linear regression models were constructed for primary and secondary outcomes to evaluate the association of ANS use after adjusting for GA, SGA, histologic chorioamnionitis, gender, race, health insurance, and center selected a priori. Adjusted odds ratios (OR) or regression coefficient estimates with 95% confidence intervals (CI) were calculated for each covariate in the models.

We evaluated the association between ANS and neonatal morbidities for each week of gestation between 29 and 33 weeks using multiple logistic regression models for the primary outcome and for the secondary outcomes that showed significant statistical interaction between GA and ANS. All reported *p* values are two-sided and *p* values less than 0.05 were considered to be statistically significant. Statistical analyses were conducted using SAS/STAT software, Version 9.4, Cary, NC.

Results

Of the 7,157 infants enrolled in the Moderate Preterm Registry, 6,419 (91%) were inborn and 638 (9%) were out-born. Among inborn infants, 5,916 infants did not have congenital anomalies. Of these 5,916 infants, data on ANS exposure were available for 5,886 infants categorized as no ANS (*n* = 676), partial ANS (*n* = 1,225), and complete ANS (*n* = 3,985).

groups. Betamethasone was the primary ANS in the study cohort, with only 55 participants receiving dexamethasone prior to delivery.

Maternal and infant characteristics of subjects exposed to no, partial, and complete ANS are described in Table 1. The no and partial ANS groups had higher GA (31.8 ± 1.4 and 31.6 ± 1.4 vs. 31.4 ± 1.4 weeks, $p < 0.001$) and lower rates of SGA (13.6 and 13.2% vs. 17.8%, $p = 0.0001$) and histological chorioamnionitis (19.9 and 21.2% vs. 28.1%, $p < 0.0001$) compared with the complete ANS group. Significant differences were also noted among no, partial, and complete ANS groups for maternal marital status, education, Medicaid insurance, hypertension, clinical chorioamnionitis, delivery mode, birth weight, and incidence of singleton versus multiple births.

Neonatal morbidities and mortality among the three groups of infants are shown in Table 2. Among the no, partial, and complete ANS groups, respectively, there were significant differences in DR resuscitation (4.1, 1.4, and 1.2%), surfactant-treated respiratory disease (26.5, 26.3, and 20%), severe ICH (3, 2, and 0.8%), and PDA (9.3, 8.2, and 6.6%). Infants exposed to a complete ANS course had lowest rates of DR resuscitation, surfactant-treated respiratory disease, severe ICH, and PDA. Multivariable analysis revealed that a complete ANS course was associated with lower surfactant-treated respiratory disease, compared with a partial ANS course (OR 0.62; 95% CI 0.52–0.74), and no ANS (OR 0.52; 95% CI 0.41–0.66). Male gender was associated with an increase in surfactant-treated respiratory disease (OR 1.39; 95% CI 1.21–1.62), whereas SGA status (OR 0.78; 95% CI 0.63–0.96), histologic chorioamnionitis (OR 0.49; 95% CI 0.41–0.59), Medicaid insurance (OR 0.85; 95% CI 0.72–0.99), and an increase of 1 week of gestation (OR 0.55; 95% CI 0.52–0.58) were associated with a lower risk of surfactant-treated respiratory disease (Fig. 1). Even a partial course of ANS was associated with lower DR resuscitation, mortality, and any ICH, but no difference in surfactant-treated respiratory disease, when compared with no ANS exposure.

We evaluated the association between ANS and neonatal morbidities for each week of GA (29–33 weeks) using multiple logistic regression models for the primary outcome (surfactant-treated respiratory disease). Although the interaction between GA and ANS was not statistically significant for the overall model for the primary outcome ([surfactant-treated respiratory disease]; $p = 0.2017$, we performed the per week analysis because it was preplanned. We also performed the per week analysis for DR intubation, because this outcome was noted to have significant interaction between GA and ANS ($p = 0.0095$). We noted persistence of this beneficial association from 29 to 33 weeks' GA; the lowest rates of surfactant-treated respiratory disease and DR intubation were associated with exposure to a complete course of ANS (Table 3).

Discussion

In this large multicenter cohort study of MPT infants, complete, partial, and no ANS were associated with significant differences in rates of neonatal morbidities. Among MPT infants, any ANS exposure was associated with lower DR resuscitation, DR endotracheal intubation, surfactant-treated respiratory disease, any ICH, severe ICH, and PDA. Infants exposed to a complete ANS course had the lowest risk of these morbidities. However, even a partial

course of ANS was associated with lower DR resuscitation, mortality, and any ICH, compared with no ANS exposure. ANS exposure was not associated with oxygen use at 28 days.

Previous studies of ANS have evaluated outcomes of preterm infants with a wide range of maturity ranging from 24 to 34 weeks' GA as a collective cohort. Outcomes of MPT infants born with differential exposure to ANS have not been reported previously. Pattinson et al performed a multicenter, double-blind, randomized controlled trial (dexamethasone or placebo) in South Africa, which included women with preterm premature rupture of membranes at 28 to 34 weeks' GA, 102 of whom (105 neonates) were in the dexamethasone group and 102 (103 neonates) in the placebo group. A trend toward fewer perinatal deaths was noted for the dexamethasone group (4 vs. 10 deaths in the dexamethasone and placebo group; $p = 0.16$, OR 0.37, 95% CI 0.09–1.34). A significant reduction in perinatal death was noted in a subgroup analysis of mothers who delivered beyond 24 hours of admission (1 vs. 7 deaths in dexamethasone and placebo group; $p = 0.047$).¹⁷ Travers and colleagues evaluated outcomes of preterm infants born with and without exposure to ANS by GA at birth in a large, prospective, multicenter study ($n = 117,941$, GA 23^{0/7}–34^{6/7} weeks).¹⁸ They noted a lower rate of early mechanical ventilation among infants born after exposure to any ANS, compared with those born without any exposure to ANS at each GA from 25 to 34 weeks. Data on whether the course of ANS was complete or incomplete was not available in this study.

MPT infants have been noted to be at risk of a range of respiratory problems, including transient tachypnea of newborn, apnea, respiratory distress, and hypoxemic respiratory failure.^{6,19} There has been variation in the definition for RDS in previous studies. We chose an objective and clinically meaningful criterion (surfactant-treated respiratory disease) as a criterion for lung maturity. Endotracheal intubation and mechanical ventilation may be associated with many complications in preterm infants including pneumothorax, bronchopulmonary dysplasia, and ventilator-associated pneumonia.^{20,21} The primary outcome of surfactant-treated respiratory disease was significantly lower in the complete ANS group, compared with no and partial ANS groups. Recent studies have noted lower incidence and severity of RDS with histologic chorioamnionitis.²² We noted a higher rate of histologic chorioamnionitis in the complete ANS group, compared with the no and partial ANS groups. However, exposure to a complete course of ANS remained independently associated with a lower rate of surfactant-treated respiratory disease, even after controlling for histologic chorioamnionitis.

We noted significant reductions in several neonatal morbidities (endotracheal intubation and resuscitation in the DR, ICH, and PDA) after ANS exposure. We found a significantly lower rate of severe ICH in the complete ANS group, compared with no and partial ANS group, although the proportions of infants undergoing imaging ranged from 49 to 57% in the three groups. Using data from the same NICHD NRN Moderate Preterm Registry, ANS administration has been previously shown to be associated with a reduction in abnormal cranial imaging.²³ Lack of a significant difference in the administration of oxygen at 28 days in the three groups could possibly be due to lack of power to assess this outcome, which is relatively uncommon among MPT infants.

A recent randomized controlled trial by Gyamfi-Bannerman et al conducted at 17 Maternal-Fetal Medicine Units Network evaluated the role of ANS administration to pregnant women at risk of “late preterm delivery (34^{0/7}–36^{5/7} weeks’ gestation) on neonatal respiratory morbidities.”²⁴ The primary outcome was a composite of treatment in the first 72 hours of age (use of continuous positive airway pressure or high flow nasal cannula for at least 2 hours, supplemental oxygen with a fraction of inspired oxygen of at least 0.30 for at least 4 hours, extracorporeal membrane oxygenation, or mechanical ventilation). The primary outcome occurred in 165 of 1427 neonates (11.6%) in the ANS group and 202 of 1400 (14.4%) neonates in the placebo group (relative risk, 0.80; 95% CI 0.66–0.97; $p = 0.02$). This study did not provide details on the differential exposure to ANS (no, partial, and complete course of ANS) on neonatal outcomes. Hypoglycemia in neonates was more common in the ANS group than in the placebo group (24 vs. 15%; $p < 0.001$).²⁴ We noted a persistence of the association between a complete course of ANS and lower surfactant-treated respiratory disease and lower DR intubation across nearly all weeks of gestation (29–33 weeks), with no trend for the reduction in the beneficial effect of ANS with an increasing GA. The current study reports the effects of ANS exposure for neonates that delivered at MPT gestation. Some neonates exposed to ANS during MPT gestation may be born at a later GA. It is possible that the beneficial and adverse effects of ANS exposure may be different for neonates delivering at more mature GA, as compared to neonates born at MPT gestation.

MPT infants represent a significant proportion of preterm infants. Moreover, these infants incur significant short- and long-term morbidities and have considerable societal and financial impact on the health care system.²⁵ Several large population-based cohort studies from Sweden and Norway have noted that MPT infants (29–32 weeks’ GA) have a significantly higher risk of disability and need for long-term assistance as compared with infants born at term gestation, and these studies found that most children and adults with special needs were born MPT.^{26,27} Our data suggest that a complete course of ANS is associated with lower neonatal morbidities including surfactant-treated respiratory disease, DR resuscitation, and ICH. Preventing these complications may, in turn, result in fewer childhood and adult disabilities.

The limitations of our study include its observational design, which permits only the identification of associations between neonatal morbidities and differential exposure to ANS and does not demonstrate causal relationships. Patients were born at the participating academic centers of the NRN, and may not be representative of the entire population. Infants born prior to receipt of a complete course of ANS might have different baseline characteristics, which could potentially be confounding factors for the differences in their outcomes. Significant differences were noted among no, partial, and complete ANS groups in GA, SGA status, histologic chorioamnionitis, maternal marital status, education, Medicaid insurance, hypertension, delivery mode, birth weight, and singleton versus multiple births. We controlled for many potential factors, however, that have been previously reported to influence neonatal morbidities, including GA, SGA status, chorioamnionitis, gender, race, health insurance, and center. We also included all eligible inborn MPT infants, born at 29^{0/7}–33^{6/7} weeks’ GA delivered at participating NRN centers in a defined time frame. We were not able to evaluate the impact of the duration between administration of the

first dose of ANS and delivery due to lack of data regarding timing of administration of ANS. Another drawback is that cranial imaging in the MPT population was not consistent and was performed in only 60% of infants. The primary outcome (surfactant-treated respiratory disease) was pragmatic and may be clinician and center dependent. Adjustment was made for the center of birth.

The strengths of our study include (1) recent, large multicenter cohort of infants; (2) use of prespecified definitions for all outcomes; and (3) prospective collection of data by trained and experienced research staff. In addition, the size of our cohort allowed us to evaluate the association of ANS with neonatal morbidities by week of GA. The study participants were from centers across the United States, with different race and socioeconomic strata, which increases the generalizability of this study. We evaluated the association of ANS exposure (no, partial, complete course) as a trichotomized variable and noted maximum benefits associated with a complete course of ANS among this MPT cohort. A dose-dependent association of ANS exposure on the outcome provides strong evidence for the benefits of ANS for MPT infants. Our group recently noted differential benefits of ANS as a trichotomized variable (no/partial/complete course of ANS) on survival, neonatal morbidities, as well as neurodevelopmental outcomes at 18 to 22 months of age among extremely preterm infants, with maximum benefits noted for the complete ANS group.²⁸ The findings of the current study may have implications for the design of trials to evaluate outcomes of MPT infants, which should take into account the differential associations of neonatal morbidities with no, partial, and complete courses of ANS. Lower neonatal morbidities associated even with a partial course of ANS in this study support the prompt administration of ANS even in situations when likelihood of receiving a complete ANS course appears low due to insufficient time.

Conclusion

In this large multicenter prospective data registry of MPT infants, ANS were associated with lower resuscitation and endotracheal intubation in the DR, surfactant-treated respiratory disease, and severe ICH with the lowest frequency of morbidities associated with a complete course. The associations between ANS and lower surfactant-treated respiratory disease, as well as intubation in the DR, persist from 29 to 33 weeks' GA. These results support recommendations to administer ANS prior to MPT birth.

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Participating NRN sites collected data and transmitted it to RTI International, the data coordinating center (DCC) for the network, which stored, managed, and analyzed the data for this study. On behalf of the NRN, Dr. Abhik Das (DCC Principal Investigator) and Mr. Dhuly Chowdhury (DCC Statistician) had full access to all of the data in the study, and with the NRN Center Principal Investigators, take responsibility for the integrity of the data and accuracy of the data analysis.

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Fig. 1.
Factors associated with surfactant-treated respiratory disease.

Table 1

Maternal and neonatal characteristics by exposure to antenatal steroids

Variable ^a mean $\pm$ SD or n (%) ^a	No ANS, <i>n</i> = 676	Partial ANS, <i>n</i> = 1225	Complete ANS, <i>n</i> = 3985	<i>p</i> -Value
Married maternal status	292/676 (43.2)	548/1224 (44.8)	1914/3983 (48.1%)	0.0177
Maternal education (>high school)	362/509 (71.1)	683/900 (75.9)	2409/2938 (82.0)	<0.0001
Maternal hypertension	123/675 (18.2)	260/1225 (21.2)	1028/3983 (25.8)	<0.0001
Clinical chorioamnionitis	27/676 (4.0)	60/1225 (4.9)	357/3983 (9.0)	<0.0001
Histologic chorioamnionitis ^b	115/579 (19.9)	230/1086 (21.2)	1002/3572 (28.1)	<0.0001
Rupture of membrane > 18 hours	74/646 (11.5)	118/1173 (10.1)	936/3765 (24.9)	<0.0001
Mode of delivery (cesarean section)	427/676 (63.2)	727/1225 (59.3)	2551/3981 (64.1)	0.0111
Multiple births	165/676 (24.4)	351/1225 (28.7)	1301/3985 (32.6)	<0.0001
Race				
White	348/640 (54.4)	663/1166 (56.9)	2228/3810 (58.5)	0.1239
Black	244/640 (38.1)	426/1166 (36.5)	1313/3810 (34.5)	0.1233
Others	48/640 (7.5)	77/1166 (6.6)	269/3810 (7.1)	0.7615
Males	373/676 (55.2)	620/1225 (50.6)	2038/3982 (51.2)	0.1219
Gestational age (weeks)	31.8 1.4	31.6 1.4	31.4 1.4	<0.0001
Birth weight (grams)	1790.1 408.5	1739.0 402.3	1661.5 411.2	<0.0001
SGA	92/676 (13.6)	162/1225 (13.2)	707/3980 (17.8)	0.0001
Medicaid insurance	432/672 (64.3)	700/1222 (57.3)	2139/3982 (53.7)	<0.0001

^aDenominator for each variable is based on availability of data.^b Among infants for whom data are available.

Neonatal morbidities among moderately preterm infants by exposure to antenatal steroids

Table 2

Variable, mean $\pm$ SD, or n (%)	No ANS, $n = 676$	Partial ANS, $n = 1,225$	Complete ANS, $n = 3,985$	Adjusted odds ratio (95% CI) or estimate (95% CI)		
				Partial versus no	Complete versus no	Complete versus partial
DR intubation ^c	131/676 (19.4)	200/1225 (16.3)	446/3983 (11.2)	0.74 (0.55–1.01)	0.46 (0.35–0.60)	0.62 (0.50–0.76)
Advanced DR Resuscitation ^{a,c}	28/676 (4.1)	17/1225 (1.4)	47/3982 (1.2)	0.40 (0.20–0.77)	0.27 (0.16–0.48)	0.69 (0.38–1.25)
Mortality ^c	11/676 (1.6)	7/1225 (0.6)	43/3985 (1.1)	0.25 (0.08–0.73)	0.58 (0.28–1.18)	2.32 (0.91–5.92)
Surfactant-treated respiratory disease ^c	179/675 (26.5)	322/1225 (26.3)	795/3984 (20.0)	0.84 (0.64–1.1)	0.52 (0.41–0.66)	0.62 (0.52–0.74)
Severe ICH ^{b,c}	10/328 (3.0)	13/652 (2.0)	18/2268 (0.8)	0.74 (0.28–1.95)	0.33 (0.13–0.81)	0.44 (0.21–0.95)
Any ICH ^c	55/328 (16.8)	76/652 (11.7)	295/2268 (13.0)	0.60 (0.38–0.93)	0.64 (0.44–0.94)	1.07 (0.80–1.44)
Oxygen use at 28 days ^c	39/643 (6.1)	77/1180 (6.5)	310/3816 (8.1)	0.96 (0.58–1.60)	1.21 (0.77–1.91)	1.26 (0.92–1.73)
Patent ductus arteriosus ^{b,c}	63/675 (9.3)	100/1224 (8.2)	262/3984 (6.6)	0.82 (0.56–1.21)	0.60 (0.43–0.85)	0.73 (0.56–0.96)
Necrotizing enterocolitis ^{b,c}	16/674 (2.4)	24/1225 (2.0)	92/3983 (2.3)	0.81 (0.40–1.64)	0.87 (0.47–1.59)	1.07 (0.66–1.73)
Early onset sepsis ^{b,d}	3/675 (0.4)	6/1225 (0.5)	25/3984 (0.6)			
Late onset sepsis ^{b,c}	14/675 (2.1)	36/1222 (2.9)	105/3975 (2.6)	1.44 (0.71–2.93)	1.16 (0.61–2.22)	0.81 (0.53–1.23)
Hospital length of stay ^e	30.7 $\pm$ 21.0 Median 27.0	31.6 $\pm$ 19.1 Median 29.0	32.9 $\pm$ 17.6 Median 31.0	0.50 (–0.90,1.90)	–0.03 (–1.06,1.01)	–0.53 (–2.09,1.04)
Postmenstrual age at hospital discharge (weeks) ^e	36.7 $\pm$ 2.6 Median 36.4	36.6 $\pm$ 2.2 Median 36.3	36.6 $\pm$ 1.9 Median 36.3	0.07 (–0.12,0.27)	0.00 (–0.15,0.15)	–0.07 (–0.30,0.15)

Abbreviations: ANS, antenatal corticosteroids; CI, confidence interval; DR, delivery room; ICH, intracranial hemorrhage; SD, standard deviation.

^aChest compression and/or epinephrine.^bNot controlled for center due to small numbers.^cAdjusted odds ratio (95% CI).^dAdjusted analysis not performed due to small sample size.^eAdjusted estimate (95% CI).

Table 3
Surfactant-treated RD and DR intubation with exposure to antenatal steroids per week of gestation

Gestational age (weeks)	No ANS, n (%)	Partial ANS, n (%)	Complete ANS, n (%)	Adjusted odds ratio (95% CI)		
				Partial versus no	Complete versus no	Complete versus partial
29 weeks: Surfactant for RD	31/60 (51.7)	79/144 (54.9)	195/458 (42.6)	1.37 (0.63–2.98)	0.74 (0.35–1.57)	0.54 (0.34–0.86)
29 weeks: DR intubation	28/60 (46.7)	54/144 (37.5)	119/458 (26.0)	1.28 (0.56–2.91)	0.61 (0.28–1.34)	0.48 (0.29–0.78)
30 weeks: Surfactant for RD	37/70 (52.9)	66/159 (41.5)	193/651 (29.6)	0.77 (0.39–1.51)	0.39 (0.21–0.72)	0.51 (0.33–0.77)
30 weeks: DR intubation	26/70 (37.1)	54/159 (34)	100/650 (15.4)	1.00 (0.49–2.03)	0.30 (0.16–0.58)	0.30 (0.19–0.47)
31 weeks: Surfactant for RD	26/89 (29.2)	76/216 (35.2%)	172/744 (23.1)	1.15 (0.62–2.14)	0.75 (0.43–1.31)	0.65 (0.44–0.95)
31 weeks: DR intubation	18/90 (20.0)	35/216 (16.2)	100/744 (13.4)	0.56 (0.26–1.20)	0.62 (0.32–1.21)	1.11 (0.66–1.85)
32 weeks: Surfactant for RD	34/168 (20.2)	50/270 (18.5)	152/983 (15.5)	0.78 (0.43–1.40)	0.61 (0.37–1.02)	0.78 (0.52–1.18)
32 weeks: DR intubation	30/168 (17.9)	33/270 (12.2)	75/983 (7.6)	0.55 (0.29–1.08)	0.37 (0.21–0.64)	0.66 (0.39–1.11)
33 weeks: Surfactant for RD	50/287 (17.4)	51/436 (11.7)	82/1147 (7.1)	0.61 (0.36–1.04)	0.35 (0.21–0.58)	0.57 (0.38–0.88)
33 weeks: DR intubation	29/287 (10.1)	24/436 (5.5)	52/1147 (4.5)	0.47 (0.25–0.91)	0.46 (0.27–0.79)	0.97 (0.55–1.70)

Abbreviations: ANS, antenatal corticosteroids; CI, confidence interval; DR, delivery room; RD, respiratory disease.