Association of Antenatal Steroid Exposure at ≤ 22 Weeks of Gestation with Survival without Severe Neurodevelopmental Impairment

NICHD
NEONATAL RESEARCH NETWORK

Sanjay Chawla M.D., Myra H. Wyckoff, M.D., Dhuly Chowdhury, MS, Matthew A. Rysavy M.D. Ph.D., Ravi Mangal Patel M.D., Rachel G. Greenberg M.D. M.B. M.H.S., Edward F. Bell M.D., Noelle E. Younge M.D., Seetha Shankaran M.D., Girija Natarajan M.D., Abbot R. Laptook M.D., Satyan Lakshminrusimha M.D., Sara DeMauro MD., Susan Hintz M.D., M.S Epi, Betty R. Vohr M.D., Krisa P. Van Meurs M.D., Namasivayam Ambalavanan M.D., Erika F. Werner M.D., Leeann R. Pavlek M.D., Carl Backes M.D., Waldemar A. Carlo M.D, for the NICHD Neonatal Research Network.

Introduction

- Antenatal steroids (ANS) given at ≤ 22 weeks' gestation are associated with decreased mortality and short-term morbidities.
- However, data are lacking on neurodevelopmental outcomes.
- Guidelines vary for providing antenatal steroids at ≤ 22 weeks.

Eligibility Criteria

- Infants born at $22^{0/7}$-$23^{6/7}$ weeks' gestation between January 2016 and December 2019 at hospitals participating in the National Institute of Child Health and Human Development Neonatal Research Network.
- Infants who did not receive intensive care and infants with ANS exposure after $22^{6/7}$ weeks' GA were excluded.

Methods

- The primary outcome was a three-level polytomous outcome including survival without severe neurodevelopmental impairment (sNDI), survival with sNDI, or death.
- Infants were classified as having no, partial (1 dose) or complete (2 doses) exposure to ANS at ≤ 22 weeks.
- Severe NDI was defined as ≥ 1 of the following: bilateral blindness, deafness, Gross Motor Function Level 4 or 5, motor and/or cognitive composite score <70 assessed using Bayley Scales of Infant and Toddler Development III at 22-26 months' corrected age.
- The association of ANS exposure and outcomes was evaluated using generalized linear mixed models for multinomial and binary outcomes, adjusting for GA, sex, race, Medicaid insurance, small for gestation (SGA), mode of delivery, multiple birth, prolonged rupture of membranes, birth year, antenatal magnesium sulfate, and birth hospital as a random effect.

Results

Outcome	Adjusted Relative Risks (95% CI)	
	Any vs. No ANS	Complete vs. No ANS
Survival without severe NDI vs. death	3.48 (1.33 - 9.10)	4.05 (1.52 - 10.78)
Survival with severe NDI vs. death	1.40 (0.48 - 4.12)	1.69 (0.66 - 4.31)
Survival without severe NDI vs. Survival with severe NDI	2.48 (0.79 - 7.81)	2.40 (0.74 - 7.80)

Conclusion

- Use of ANS at ≤ 22 weeks gestation may improve survival without neurodevelopmental impairment for extremely preterm infants and reduce the risk of moderate-severe CP among survivors

https://Neonatal.RTI.org/Publications/

Results

Maternal and Neonatal Characteristics by Exposure to ANS

Variable	Complete ANS Course, n= 219	Partial ANS course, n= 73	No ANS n= 103	P-Value
Maternal education (>high school)	64%	43%	43%	<0.01
Maternal Magnesium exposure	81%	64%	14%	<0.01
Clinical chorioamnionitis	24%	19%	14%	0.08
Histologic chorioamnionitis	79%	80%	58%	<0.01
Cesarean delivery	45%	11%	30%	<0.01
Singleton	67%	73%	72%	0.50
Hispanic ethnicity	11%	8%	35%	<0.01
Race				
White	48%	30%	56%	<0.01
Black	47%	63%	42%	0.02
Other	5%	7%	2%	0.31
Males	58%	47%	55%	0.26
Gestational age (weeks)	23 (22-23)	22 (22-22)	23 (22-23)	<0.01
Birth weight (grams)	546 (490-605)	532 (469-581)	540 (495-620)	0.30
Medicaid Insurance	47%	64%	63%	<0.01
Apgar score 1 minute	2 (1-4)	1 (1-3)	1 (1-2)	<0.01
Apgar score 5 minute	5 (3-7)	4 (1-6)	3 (1-5)	<0.01

P value refers to unadjusted test for differences using chi-square test for categorical variables, Wilcoxon test for continuous variables

Neurodevelopmental Outcome of Children Born at 22-23 weeks' GA after a Complete course, Partial course or no Exposure to ANS at ≤ 22 weeks

Variable	(%)			Adjusted Relative Risks (95% CI)	
	Complete ANS	Partial ANS	No ANS	Any vs. No ANS	Complete vs. No ANS
Survival without severe NDI	**35%**	**18%**	**14%**	**2.54 (1.17 to 5.53)**	**2.72 (1.23 to 6.02)**
Survival with severe NDI	13%	11%	16%	1.00 (0.47 to 2.12)	1.11 (0.50 to 2.43)
Death	52%	70%	69%	0.75 (0.51 to 1.09)	0.70 (0.47 to 1.04)
Severe NDI among survivors	27%	38%	53%	0.56 (0.25 to 1.25)	0.58 (0.25 to 1.33)
Moderate to severe CP*	**9%**	**18%**	**38%**	**0.20 (0.06 to 0.60)**	**0.16 (0.05 to 0.54)**
Moderate to severe CP or death	**56%**	**75%**	**81%**	**0.70 (0.49 to 1.00)**	**0.65 (0.44 to 0.95)**
BSID III Cognitive Score <70*	26%	33%	52%	0.52 (0.23 to 1.19)	0.57 (0.24 to 1.33)
BSID III Cognitive <70 or death	65%	81%	85%	0.79 (0.56 to 1.10)	0.76 (0.53 to 1.09)
BSID III Language Score <70*	41%	40%	58%	0.73 (0.35 to 1.52)	0.76 (0.35 to 1.62)
BSID III Language <70 or death	72%	83%	87%	0.83 (0.59 to 1.16)	0.81 (0.57 to 1.15)
BSID III Motor Score <70*	29%	32%	63%	0.48 (0.22 to 1.04)	0.50 (0.22 to 1.14)
BSID III Motor Score <70 or death	67%	80%	89%	0.76 (0.54 to 1.07)	0.74 (0.52 to 1.05)

* Among survivors

Limitations

- There is a possibility of difference in unknown confounders associated with both the decision to provide ANS and neonatal care.

Disclosures: The authors have no financial relationships to disclose or conflicts of interest to resolve. Any real or apparent conflicts of interest related to the content of this poster have been resolved. This poster does not involve discussion of unapproved or off-label, experimental or investigational use of a drug.

Acknowledgements: The National Institutes of Health and the Eunice Kennedy Shriver National Institute of Child Health and Human Development provided grant support for the Neonatal Research Network. We are indebted to the infants and their parents who agreed to take part in this study and to our medical and nursing colleagues at: Brown University; Case Western Reserve University; Cincinnati Children's Hospital Medical Center; Duke University; Emory University; Nationwide Children's Hospital/Ohio State University, RTI International; Stanford University; University of Alabama at Birmingham; University of Iowa; University of New Mexico; University of Pennsylvania, University of Rochester; University of Texas Southwestern Medical Center; University of Texas Health Science Center at Houston; University of Utah.

NIH Eunice Kennedy Shriver National Institute of Child Health and Human Development