Effect of Hydrocortisone (HC) on Cardiac Mass in Preterm Intubated Infants < 30 weeks Gestational Age

NICHD
NEONATAL RESEARCH NETWORK

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Introduction

- Dexamethasone use in preterm infants has been associated with adverse effects including hypertension, and an increase in the left ventricular mass index (LVMI), a surrogate for left ventricular hypertrophy.
- There are few data on the effects of hydrocortisone (HC) on cardiac mass and function.
- An increased LVM is a risk factor for cardiovascular morbidity.

Eligibility Criteria

- Prospective secondary study of a subset of infants in the NICHD Neonatal Research Network RCT, "Hydrocortisone to Improve Survival without Bronchopulmonary Dysplasia" (N Engl J Med 2022; 386:1121).
- Infants eligible for the RCT were < 30 weeks' gestation without major congenital anomaly, 14-28 days postnatal age, intubated, and had received ≥ 7 days of mechanical ventilation.
- Infants were randomized to a 10-day tapering course of HC from 4mg/kg/day or placebo.

Objectives

- (1) To determine if HC therapy in preterm ventilated neonates is associated with an increase in the LVMI at 36 weeks postmenstrual age (PMA) compared to placebo;
- (2) to compare the incidence of pulmonary hypertension at 36 weeks PMA between these groups

Methods

- The primary outcome was left ventricle mass index (LVMI) on echocardiogram at 36 weeks PMA, read by a central reader masked to group assignment.
- A sample size of 124 was needed to detect a 10% difference in the primary outcome (LVMI) .
- Secondary outcomes were pulmonary hypertension, systolic blood pressure, and cardiac wall thickness.

Results

Outcome	Hydrocortisone n=61	Placebo n=67	Adjusted p value##
Left Ventricle Mass Index* M mode	49.3 (10.8)	53.1 (14.7)	0.03
Left Ventricle Mass Index 2-D method	34.7 (13.2)	38.3 (6.9)	0.04
Pulmonary Hypertension#	3/61 (4.9)	6/67 (9.0)	0.37
Systolic blood pressure mm Hg	76.5 (10.8)	77.52 (11.4)	0.44
Posterior cardiac wall thickness, cm	0.4 (0.06)	0.4 (0.05)	0.45

Patient Characteristics**

Variable	Hydrocortisone, n=61	Placebo, n= 67
Birth weight (grams), mean (SD)	667 (125)	736 (182)
Gestational age (weeks), median (P25 P75)	25.0 (24.0, 26.0)	25.0 (24.0, 26.0)
Male sex n/N (%)	27/61 (44)	40/67 (59.7)
5-minute Apgar score, median (P25 P75)	6.0 (3.0, 7.0)	6.0 (4.0, 7.0)
Small for gestational age, n/N	9/61 (15)	4/67 (6.0)
Any open label postnatal steroids, n/N (%)[1]	28/61 (46)	29/66 (43.9)
Highest mode of respiratory support at randomization, n/N		
HFV	11/61 (18)	17/67 (25.4)
CV	50/61 (82)	50/67 (74.6)
NIPPV	0/61 (0.0)	0/67 (0.0)
FiO2 at trial entry, Mean (SD)	51.9 (20)	51.1 (20.4)
Respiratory index at trial entry (MAP XFiO2 X100), Mean (SD)	566 (306)	589 (362)
PMA at Echocardiogram, median (P25, P75)	36.0 (36.0, 36.0)	36.0 (35.0, 36.0)
Medications given on day of echo, n/N (%)		
Diuretics	23/61 (38)	29/67 (43)
Systemic steroids	5/61 (8)	5/67 (7)
Bosentan or Sildenafil	0/61 (0.0)	2/67 (3.0)

Neonatal Characteristics at the time of Echocardiogram

Variable	Hydrocortisone, n=61	Placebo, n= 67	Adjusted p value
IVSd cm: N, mean (SD)	61, 0.33 (0.05)	67, 0.33 (0.04)	0.21
LVIDd cm: N, mean (SD)	61, 1.64 (0.21)	67, 1.73 (0.20)	<.01
PWDd cm: N, mean (SD)	61, 0.32 (0.04)	67, 0.33 (0.04)	0.04
LVIDs cm: N, mean (SD)	61, 1.00 (0.16)	67, 1.08 (0.17)	<.01
Systolic to diastolic duration ratio: N, mean (SD)	58, 1.45 (0.30)	1.43 (0.27)	0.99
High RV systolic pressure, n/N (%)*	3/8 (37)	5/10 (50)	0.57
Patent ductus arteriosus, n/N (%)	9/61 (15)	12/67 (18)	0.64
Tricuspid regurgitation (TR) Jet present, n/N	9/61 (15)	10/67 (15)	0.97

** No substantive differences in patient characteristics observed between the overall trial cohort and the current subset studied

Conclusions

- Among extremely preterm infants, a 10-day tapering course of HC initiated between 2 and 4 weeks postnatal age, was associated with lower LVMI at 36 weeks PMA, compared to placebo.
- Long term clinical significance of this change should be explored.
- No significant functional or structural adverse cardiac effects were seen with use of 10-day course of postnatal hydrocortisone.

- *Defined as those whose TR jet RVSP divided by systemic systolic blood pressure is > 0.5.
- IVSD: Interventricular septal dimension during diastole
- LVIDd: Left ventricular internal dimension during diastole
- PWDd: Posterior wall dimension during diastole
- LVIDs: Left ventricular internal dimension during systole

*Left ventricle mass index (LVMI) was calculated by dividing LVM by body surface area
#One or more of the following: one or more of: high RV systolic pressure, bi-directional or R to L shunting, or atrial septal flattening or bowing.
##For both continuous and categorical variables, all models were adjusted for the trial stratification factors of center and gestational age strata.
For the categorical variables, a collapsed version of center was used in order to achieve model convergence.

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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.

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