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Early postnatal hypotension is not associated with indicators of white matter damage or cerebral palsy in extremely low gestational age newborns

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Abstract

Objectives—To evaluate, in extremely low gestational age newborns (ELGANs), relationships between indicators of early postnatal hypotension and cranial ultrasound indicators of cerebral white matter damage imaged in the nursery and cerebral palsy diagnoses at 24 month follow-up.

Methods—The 1041 infants in this prospective study were born at < 28 weeks gestation, were assessed for 3 indicators of hypotension in the first 24 postnatal hours, had at least one set of protocol cranial ultrasound scans, and were evaluated with a structured neurologic exam at 24 months corrected age. Indicators of hypotension included: 1) lowest mean arterial pressure (MAP) in the lowest quartile for gestational age; 2) treatment with a vasopressor; and 3) blood pressure lability, defined as the upper quartile of the difference between each infant's lowest and highest

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Conflict of Interest Statement

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MAP. Outcomes included indicators of cerebral white matter damage, i.e. moderate/severe ventriculomegaly or an echolucent lesion on cranial ultrasound, and cerebral palsy diagnoses at 24 months gestation. Logistic regression was used to evaluate relationships among hypotension indicators and outcomes, adjusting for potential confounders.

Results—Twenty-one percent of surviving infants had a lowest blood pressure in the lowest quartile for gestational age, 24% were treated with vasopressors, and 24% had labile blood pressure. Among infants with these hypotension indicators, 10% percent developed ventriculomegaly and 7% developed an echolucent lesion. At 24-months follow-up, 6% had developed quadriparesis, 4% diparesis, and 2% hemiparesis. After adjusting for confounders, we found no association between indicators of hypotension, and indicators of cerebral white matter damage or a cerebral palsy diagnosis.

Conclusions—The absence of an association between indicators of hypotension and cerebral white matter damage and or cerebral palsy suggests that early hypotension may not be important in the pathogenesis of brain injury in ELGANs.

Keywords

hypotension; mean arterial blood pressure; cranial ultrasound; ventriculomegaly; echolucent lesion; cerebral palsy; extremely preterm infants

Introduction

In a multi-center study, we found that more than 80% of extremely low gestational age newborns (ELGANs) were given some treatment to increase blood pressure,[1] perhaps because it has been posited that hypotension causes brain damage in preterm newborns.[2] One indicator of brain damage, cranial ultrasound abnormalities, has been associated with systemic hypotension in several studies. [3–9] However, the majority of published studies found no such association.[10–22] Conflicting results have also been obtained from studies of the association between hypotension and cerebral palsy.[22–25] Moreover, there appears to be uncertainty about whether treatments for hypotension in preterm newborns are beneficial or harmful.[9, 21] In summary, the literature is unclear about the relationship between systemic hypotension, its treatment, and brain damage in preterm newborns.

The ELGAN Study provided the opportunity to evaluate relationships between three indicators of hypotension during the first 24 postnatal hours, cranial ultrasound lesions observed during initial hospitalization, and a cerebral palsy diagnosis 24 months later.

Methods

The ELGAN Study was designed to identify characteristics and exposures that increase the risk of structural and functional neurological disorders in ELGANs (Extremely Low Gestational Age Newborns).[26] During the years 2002–2004, women whose babies were delivered before 28 weeks gestation at one of 14 participating institutions were asked to enroll in the study. The project was overseen by the National Institutes of Health, the institutional review boards of the 14 participating institutions, and an external Performance Monitoring and Safety Board (members appointed by the National Institutes of Neurologic

Disorders and Stroke) at Children's Hospital Boston. All variables and outcomes were defined prospectively. The original ELGAN Study included training for research personnel prior to the start of the study, and multiple training sessions were held to ensure consistent approaches to data collection. As such, this is a secondary analysis of prospectively acquired data from the original sample of 1506 infants, born in 14 level III neonatal intensive care units in the United States.

The sample of 1041 infants who are the subjects of this analysis had all three day-1 hypotension measures, one or more protocol ultrasound sets, and a neurologic exam at 24 months corrected age (Figure 1). To assess bias, we compared characteristics of the infants who returned for a developmental assessment to those of the 142 infants who were eligible but did not return. Infants who returned for 24 month follow-up tended to be born later in gestation but were more likely to have one of the indicators of hypotension.

Demographic, pregnancy and delivery variables

The clinical circumstances that led to each maternal admission and ultimately to each preterm delivery were operationally defined using data from a structured maternal interview and data abstracted from the medical record.[27] Characteristics and exposures which were evaluated as potential confounders are shown in Table 2.

Newborn variables

Gestational age estimates were based on a hierarchy of the quality of available information. Most desirable were estimates based on the dates of embryo retrieval, intrauterine insemination or fetal ultrasound before the 14th week (62%). When these were not available, reliance was placed sequentially on a fetal ultrasound at 14 or more weeks (29%), date of the last menstrual period without fetal ultrasound (7%), and gestational age recorded in the log of the neonatal intensive care unit (1%). The birth weight Z-score and head circumference Z-score represent the number of standard deviations the infant's weight or head circumference are above or below the mean of infants at the same gestational age in a standard data set.[28]

Hypotension indicators

The ELGAN Study recorded three mean arterial blood pressures--the lowest, highest, and mode (most common)--during the first 24 postnatal hours. Because no single definition of hypotension is widely accepted,[1, 20] we examined three indicators of hypotension: 1) lowest mean arterial pressure (MAP) in the lowest quartile for gestational age (23–24, 25–26, and 27 weeks); 2) treatment for hypotension with a vasopressor (dopamine, dobutamine, or epinephrine); and 3) blood pressure lability, defined as the upper quartile of the difference between the lowest and highest MAP.

The first definition of hypotension, "lowest MAP in the lowest quartile for gestational age" is based on the distribution of the lowest recorded MAPs in the sample. The second definition, "vasopressor treatment", is an operational definition that derives from the assumption that hypotension was important enough to treat, regardless of how the clinician arrived at that decision. The third definition, "blood pressure lability", makes use of the

lowest and highest blood pressures in the sample, and reflects the portion of the sample with the greatest variability in recorded MAPs.

Clinicians and researchers frequently use MAP (in mmHg) less than gestational age (in weeks) as a definition for hypotension.[20, 29] Using that definition, approximately two-thirds of infants in this cohort were "hypotensive" making it difficult to evaluate its potential impact. Similarly, since 75% of the cohort received volume expansion in the first 24 postnatal hours, volume expansion was not used as an indicator of hypotension in this study.

We did not specify *a priori* the method for measuring blood pressure (oscillometry or intra-arterial catheter) or a frequency with which pressures were to be recorded and research personnel who abstracted data were unaware of the method.

Cranial ultrasound evaluation

In this sample of ELGANs, moderate/severe ventriculomegaly and an echolucent lesion were better predictors of cerebral palsy and developmental delay than echodensity.[30, 31] In addition, the inter-reader agreement was higher for moderate/severe ventriculomegaly and an echolucent lesion than for echodensity.[30] Therefore, we chose moderate/severe ventriculomegaly and an echolucent lesion as *indicators of white matter damage*; hereafter, all references to "indicators of white matter damage" indicate moderate/severe ventriculomegaly and/or an echolucent lesion on postnatal ultrasound.

The three sets of protocol scans were defined by the postnatal day on which they were obtained. Protocol 1 scans were obtained between the first and fourth day (N=784), protocol 2 scans were obtained between the fifth and fourteenth day (N=973), and protocol 3 scans were obtained between the fifteenth day and the 40th week (N=1011). Seven hundred eleven infants in this sample of 1041 had all three sets of ultrasound studies.

Details about the methods for obtaining ultrasound scans, efforts to minimize observer variability, and strategies aimed at achieving concordance in the reading of the ultrasound scans are described elsewhere.[32] All ultrasound scans were read by two independent sonologists who were not provided clinical information. When the two readers differed in their recognition of moderate/severe ventriculomegaly or an echolucent lesion, the films were sent to a third (tie-breaking) reader who was unaware of the first two sonologists reports.

Neurologic assessment

A developmental assessment was offered to all survivors at 24 months corrected gestational age. Of the study participants alive at 24 months, 88% were evaluated with a neurologic exam. The developmental assessment included a 31-item structured neurologic examination administered by staff who were trained and certified using a multi-media training video.[33] Due to the low frequency of non-spastic cerebral palsy in infants less than 2 years of age, we focused on the spastic forms of cerebral palsy (quadriparesis, diparesis, or hemiparesis) using a previously published algorithm.[34] The referenced algorithm includes monoparesis under the classification hemiparesis, and triparesis under the classification quadriparesis.

Data analysis

We evaluated the null hypothesis that infants with an indicator of hypotension during the first 24 postnatal hours were no more likely than their peers to have an indicator of white matter damage or a cerebral palsy diagnosis.

To identify potential confounders, we compared the distribution of characteristics and exposures among children who had each hypotension indicator to the distribution among those who did not. We then compared the distribution of these characteristics and exposures among children who did and did not have each of the outcomes.

Characteristics and exposures of the pregnancy, delivery, and postnatal period were treated as potential confounders if they had been considered potential confounders previously, or were associated in this dataset with both the exposure (a hypotension indicator) and the outcome (a cranial ultrasound lesion or cerebral palsy diagnosis) with a p-value ≤ 0.25. The only exception to the foregoing was that we did not treat SNAP-II (Score for Neonatal Acute Physiology-II) as a potential confounder because lowest MAP in the first 12 hours is a component of SNAP-II.[35] We fit 15 separate multivariate logistic regression models, one for each of the five outcomes with each of the three hypotension indicators. In order to study the most homogeneous outcomes, we compared children with each CP diagnosis to those without CP. Each model included a hospital strata term to account for the possibility that infants born at a particular hospital were more like each other than like infants born at other hospitals. We describe the strength of the association between indicators of hypotension and indicators of white matter damage and cerebral palsy diagnosis, by calculating odds ratios (OR) and 95% confidence intervals (CIs), adjusting for confounders.

Results

For the parent study sample of 1506 infants, hypotension measures and cranial ultrasound scans were available for 1411 (94%). At 24 months adjusted age, 1183 (84%) of these infants were alive, and 1041 (88%) of these were evaluated with the structured neurologic exam (Figure 1). To evaluate whether there was bias due to the exclusion of the 142 infants lost to follow-up, we compared characteristics of mothers and infants who returned for a developmental assessment to those of mothers and infants who were eligible but did not return. Infants who returned for 24 month follow-up tended to be born to mothers with at least a college education, and were more likely to have a hypotension indicator (Table 1).

While the frequency of lowest blood pressure in the lowest quartile was 25% for the entire cohort, it was only 21% in the cohort for these analyses. Twenty-four percent were treated with vasopressor, and 24% had labile blood pressure. In the NICU, 10% developed moderate/severe ventriculomegaly and 7% developed an echolucent lesion. At 24-months, 6% had developed quadriparesis, 4% diparesis, and 2% hemiparesis.

Social, demographic, and pregnancy characteristics (Table 2)

We created Tables 1 and 2 to examine potential confounders of relationships between indicators of hypotension and indicators of cerebral white matter damage and cerebral palsy diagnoses. Black race and public insurance were associated with a slightly higher rate of

blood pressure lability, but infants whose mother had these characteristics were no more likely than their peers to develop cranial ultrasound lesions or a cerebral palsy diagnosis. Infants of multi-fetal gestation were more likely singletons to receive vasopressors, but were no more likely than their peers to develop one of the outcomes of interest. Maternal vaginitis was associated with blood pressure lability and with both ventriculomegaly and quadriplegia. Similarly, infants whose mothers used aspirin were more likely to have received vasopressors and more likely to develop ventriculomegaly, an echolucent lesion, and quadriplegia. However, these associations were based only on 57 women-infant dyads exposed to antenatal aspirin. Infants exposed antenatally to magnesium had lower risks of blood pressure in the lowest quartile for gestational age, and were less likely to develop ventriculomegaly, an echolucent lesion, quadriparesis, and hemiparesis.

Infant characteristics (Table 3)

Infants of low gestational age were more likely than their gestationally-older peers to receive vasopressors and to have labile blood pressure, and were slightly more likely to develop ventriculomegaly, an echolucent lesion, or a cerebral palsy diagnosis. A birth weight Z-score < -1 was associated with both labile blood pressure and hemiparesis.

Univariate relationships among hypotension indicators, indicators of white matter damage and cerebral palsy diagnoses. (Table 4)

The indicators of hypotension are highly related. Among children with a lowest blood pressure in the lowest quartile for gestation, 44% received a vasopressor, and 42% had labile blood pressure. In contrast, among those who did not have a blood pressure in the lowest quartile for gestational age, only 19% received a vasopressor and 19% had labile blood pressure.

Multivariate relationship (Figures 2 and 3)

Univariate analyses (Tables 2 and 3) identified black race, public insurance, primigravida, male sex, gestational age 23–24 weeks, birthweight Z-score < -1, multi-fetal pregnancy, delivery for preeclampsia or fetal indication, receipt of magnesium, and SNAP-II, as potential confounders. After adjusting for confounders, we found no association between any of the three indicators of hypotension and the two indicators of white matter damage (figure 2) or any of three cerebral palsy diagnoses (figure 3). SNAP-II was not included in multivariate analyses for the reasons cited in the Data analysis section.

Discussion

In a large sample of ELGANs, we found little evidence for an association between hypotension indicators and indicators of white matter damage or a cerebral palsy diagnosis. Our findings cast doubt on the concept that early postnatal hypotension, in isolation, causes brain damage in ELGANs. In addition, we did not find support for the notion that vasopressors benefit preterm neonates with early postnatal hypotension.[36]

Prior studies favoring an association between hypotension and brain ultrasound lesions[3–9] had relatively small sample sizes, decreasing the likelihood that potential confounders could

be adequately controlled. Most of the studies favoring an association between hypotension and cerebral palsy acquired data retrospectively, [9, 21, 23, 24] increasing the possibility of ascertainment bias, and the one prospective study with a design comparable to ours failed to demonstrate such an association.[25] Our findings are in agreement with the majority of published studies, which found no convincing relationship between hypotension and brain ultrasound images[10–22] or cerebral palsy.[22, 25]

The hypothesis that "early postnatal hypotension causes white matter damage in preterm infants" is predicated on two related concepts. The first is that cerebral white matter damage is a consequence of ischemia. The second is that ischemia results from systemic hypotension. Since the late 1970s, when Hans Lou published his historically important studies of preterm infants, in which early systemic hypotension was correlated with low cerebral blood flow and brain injury, neonatologists have been concerned about the adverse effects of early systemic hypotension on the fragile preterm brain.[37, 38] Since that time, it has become increasingly clear that the etiology of brain damage in preterm newborns is multifactorial.[15, 39, 40] Our study and others suggest that systemic hypotension, as an isolated clinical event, is an insufficient indicator of white matter damage in preterm newborns, and by extension, an insufficient indicator of cerebral ischemia.

We offer a number of possible explanations for why early postnatal hypotension might not increase the risk of white matter damage or cerebral palsy in extremely preterm infants. First, a relatively low blood pressure on the first day of life might be part of the normal physiologic transition from intrauterine to extrauterine life. Second, "hypotension", as described here, might not lead to cerebral ischemia. Third, if "hypotension" does cause ischemia, then it does not occur with enough frequency or severity to be associated with white matter damage or cerebral palsy at 2 years. Fourth, if hypotension is associated with white matter damage, then our crude methods for obtaining blood pressure measurements are insufficient for clinical decision-making regarding cerebral perfusion.

Our study has several limitations. First, we did not pre-specify a protocol for measuring blood pressure; some measurements were obtained by intra-arterial catheters, while others were obtained by oscillometry. Overestimates of blood pressure, which frequently accompany the use of oscillometry, might have attenuated associations between hypotension indicators and ultrasound lesions or cerebral palsy.[41, 42] Second, our findings may have been confounded by the frequent use of volume expansion. Any inferences from our findings should be limited to cohorts in which volume expansion is used frequently, as three-fourths of study infants were treated with volume expansion in the first 24 postnatal hours. Third, we might have failed to identify hypotension-related white matter damage because cranial ultrasound fails to detect some of the white matter damage that is later identified with magnetic resonance imaging.[43]

The strengths of our study include the prospective collection of data from a large multicenter cohort, defined by gestational age (rather than birth weight).[44] This study derives from a large sample of ELGANs from several regions of the United States, increasing the validity and generalizability of our findings.[45, 46] We assessed brain damage using both structural and functional outcomes that were assessed with a high degree of reliability, enhancing the

validity of these assessments. In addition, the identification of ultrasound lesions required the agreement of two independent readers, decreasing the likelihood of inter-observer variability. Finally, follow up data were collected by examiners trained in the standardized administration of the neurologic exam, and these examiners were unaware of the child's clinical history.[33]

Prior studies that provided evidence for an association between low blood pressure and white matter damage or cerebral palsy were smaller than ours, and less likely to adequately adjust for confounders. This underscores the importance of our findings, as prior "positive" studies, may have created a distorted perception of the strength of antecedent risks.[45, 46] Thus, we support the recommendation of others, that randomized trials be used to evaluate the benefit of treatments to raise blood pressure in extremely preterm neonates.[47] Perhaps the most important implication for clinicians is that our study and others fail to find support for the hypothesis that white matter damage is associated with low blood pressure in the early postnatal period.

In conclusion, in a cohort of preterm infants, the majority of whom were treated with volume expanders, we found little evidence for an association between early indicators of postnatal hypotension and two indicators of cerebral white matter damage and cerebral palsy diagnoses at 24 months corrected gestational age.

Abbreviations

ELGAN	extremely low gestational age newborn
IVH	intraventricular hemorrhage
MAP	mean arterial pressure
CP	cerebral palsy
CUS	cranial ultrasound

Hypotension.BSID Bibliography

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University Health Systems of Eastern Carolina, Greenville NC (Stephen Engelke, Ira Adler, Sharon Buckwald, Rebecca Helms, Kathyrn Kerkering, Scott S. MacGilvray, Peter Resnik)

U Mass Memorial Health Center, Worcester, MA (Francis Bednarek, Jacqueline Wellman, Robin Adair, Richard Bream, Alice Miller, Albert Scheiner, Christy Stine)

Wake Forest University Baptist Medical Center and Forsyth Medical Center, Winston-Salem NC (T. Michael O'Shea, Barbara Specter, Deborah Allred, Don Goldstein, Gail Hounshell, Robert Dillard, Cherrie Heller, Debbie Hiatt, Lisa Washburn)

William Beaumont Hospital, Royal Oak MI (Daniel Batton, Chung-ho Chang, Karen Brooklier, Melisa Oca)

Yale University School of Medicine, New Haven CT (Richard Ehrenkranz, Cindy Miller, Nancy Close, Elaine Romano, Joanne Williams)

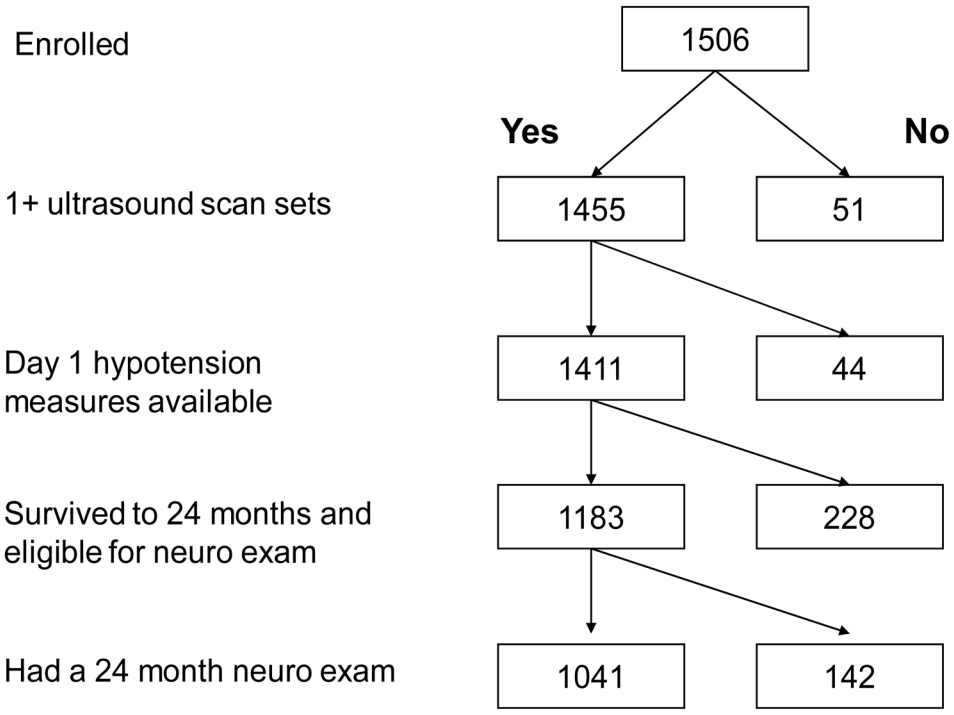

Figure 1.
Sample for analyses of hypotension indicators and ultrasound lesions and cerebral palsy

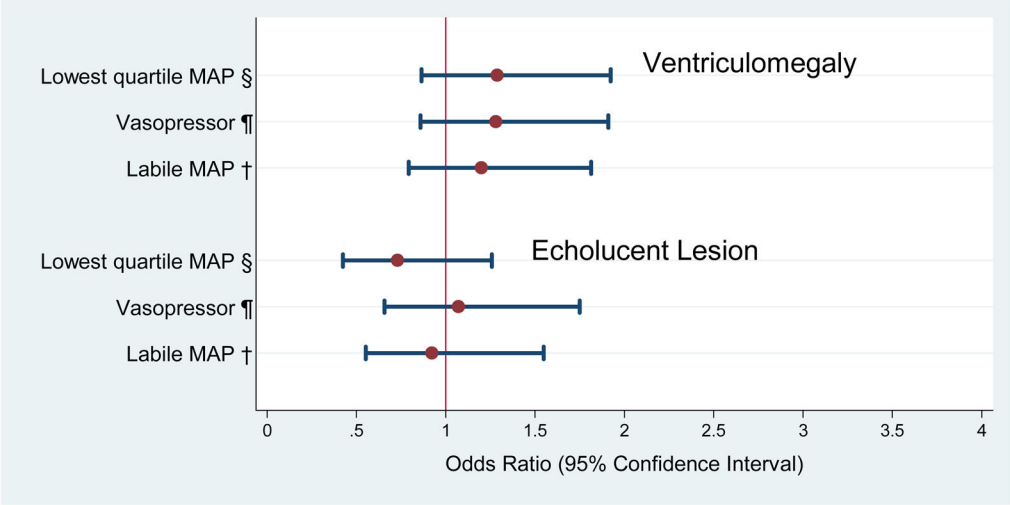

Figure 2.

Odds ratios (and 95% confidence intervals) of the risk of indicators of white matter damage obtained with logistic regression models that incorporate indicators of hypotension during the first 24 postnatal hours and potential confounders.*

*Adjustment is made for black race, public insurance, primagravida, male sex, gestational age 23–24 weeks, birth weight Z-score < -1, multi-fetal gestation, delivery for preeclampsia or fetal indication and receipt of magnesium. A hospital strata term is included to account for the possibility that infants born at a particular hospital are more like each other than like infants born at other hospitals.

§Low Q: lowest MAP recorded in the first 24 hours in the lowest quartile for gestational age

¶Vaso: treatment for hypotension with a vasopressor in the first 24 hours with any vasopressor (dopamine, dobutamine, and epinephrine)

†Labile: labile blood pressure, defined as the upper quartile of the difference in the lowest and highest MAP

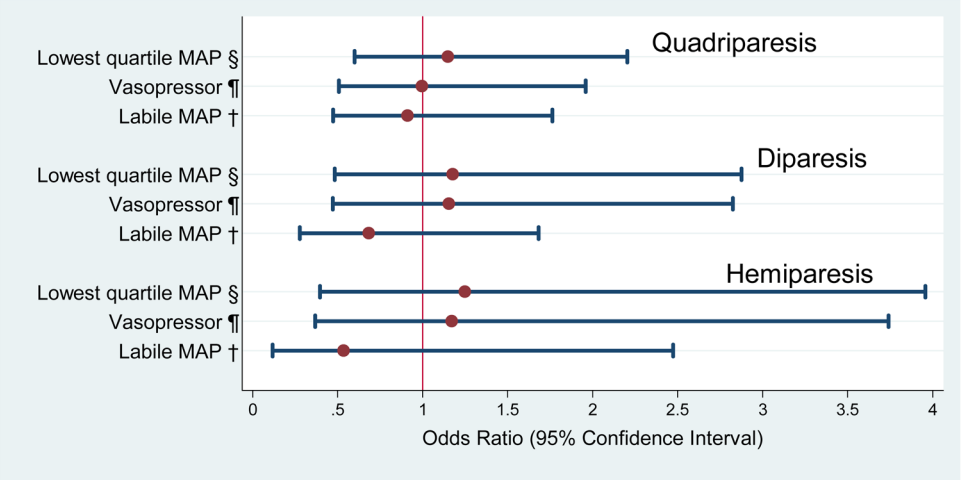

Figure 3.

Odds ratios (and 95% confidence intervals) of the risk of cerebral palsy types obtained with logistic regression models that incorporate indicators of hypotension during the first 24 postnatal hours and potential confounders.*

*Adjustment is made for black race, public insurance, primagravida, male sex, gestational age 23–24 weeks, birth weight Z-score < -1, multi-fetal gestation, delivery for preeclampsia or fetal indication and receipt of magnesium. A hospital strata term is included to account for the possibility that infants born at a particular hospital are more like each other than like infants born at other hospitals.

§Low Q: lowest MAP recorded in the first 24 hours in the lowest quartile for gestational age

¶Vaso: treatment for hypotension with a vasopressor in the first 24 hours with any vasopressor (dopamine, dobutamine, and epinephrine)

†Labile: labile blood pressure, defined as the upper quartile of the difference in the lowest and highest MAP

Table 1

Characteristics of mothers and children who survived to 24 months adjusted age, comparing those included in this study and those not included (column percents).

Maternal or infant characteristic		Included in study	Not included
Maternal education	College or more	34	22
HMO/private insurance	Yes	62	54
10+ prenatal care visits	Yes	30	27
Conception assistance	Yes	22	17
White race	Yes	59	54
Antenatal corticosteroid	Complete course	65	57
	Partial Course	25	35
	None	11	7
Cesarean delivery	Yes	66	65
Sex	Male	52	52
Gestational age (weeks)	23–24	20	23
	25–26	46	47
	27	34	30
Birth weight (grams)	≤ 750	37	37
	751–1000	44	38
	> 1000	19	25
Ventriculomegaly	Yes	10	8
Echolucent lesion	Yes	7	5
Lowest quartile MAP	Yes	21	15
Vasopressor	Yes	24	21
Labile MAP	Yes	24	18
Maximum number of infants		1041	142

[§]Lowest quartile MAP: lowest MAP recorded in the first 24 hours, in the lowest quartile for gestational age

[¶]Vasopressor: treatment for hypotension in the first 24 hours, using any vasopressor (dopamine, dobutamine, epinephrine)

[†]Labile MAP: labile blood pressure, defined as the upper quartile of the difference between the lowest and highest MAP

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Table 2

Maternal characteristics, indicators of hypotension, and indicators of white matter damage and cerebral palsy diagnoses (row percents).

Characteristics of the mother		Hypotension indicators			Indicators of white matter damage		Cerebral palsy			N
		Low Q[§]	Vaso[¶]	Labile[†]	VM	EL	Q	D	H	
Years of education	< 12	25	23	22	11	8	5	2	2	161
	12 (HS)	21	21	25	7	7	6	5	1	267
	>12 to <16	19	21	27	14	10	8	4	4	240
	College grad	19	26	23	9	4	4	3	1	187
	> 16	22	33	21	11	5	8	1	1	152
Married	Yes	19	25	22	11	7	7	3	1	609
	No	23	23	27	9	7	6	5	2	432
Black race	Yes	26	25	30	11	8	6	5	3	278
	No	19	24	21	10	7	6	3	1	747
Public insurance	Yes	23	22	29	9	8	7	5	1	397
	No	19	25	21	11	7	6	3	2	624
Primigravida	Yes	22	27	21	10	5	6	3	1	410
	No	20	22	26	11	8	7	4	2	605
Multi-fetal gestation	Yes	20	30	19	11	7	7	3	2	354
	No	21	21	26	9	7	6	4	3	687
Pre- pregnancy BMI	< 18.5	21	22	28	9	7	9	4	0	76
	18.5, <25	19	24	23	11	8	6	4	2	506
	25, <30	23	26	26	8	8	6	3	1	207
	≥ 30	24	24	24	13	5	6	2	2	211
Vaginitis	Yes	20	21	29	13	8	10	5	2	143
	No	21	24	23	10	7	6	3	2	870
Aspirin	Yes	21	30	23	18	14	19	2	0	57
	No	21	23	24	10	6	6	4	2	953
Pregnancy complication	PTL	20	25	22	13	9	6	4	3	464
	pPROM	21	23	23	10	7	6	4	2	230

Characteristics of the mother		Hypotension indicators			Indicators of white matter damage		Cerebral palsy			N
		Low Q[§]	Vaso[¶]	Labile[†]	VM	EL	Q	D	H	
	Preeclampsia	18	18	26	5	2	5	1	1	137
	Abruption	25	24	32	6	1	3	3	2	113
	Cx insuffcncy	23	35	22	9	7	15	5	0	55
	Fetal Indicatn	19	21	18	10	12	10	2	0	42
Mod/severe chorioamnionitis	Yes	19	20	23	12	9	8	6	2	343
	No	22	26	24	10	6	5	2	2	606
Antenatal steroids	Yes	21	26	24	9	7	7	4	2	672
	No	15	20	24	10	5	4	3	3	255
Magnesium	No	31	24	24	19	11	8	4	8	112
	Tocolysis	20	27	22	9	7	5	3	2	562
	Sz prophylax	21	18	28	6	2	5	3	2	133
Max number of infants		216	252	247	105	73	64	37	19	1041
Row percent		21	24	24	10	7	6	4	2	

[§]Low Q: lowest MAP recorded in the first 24 hours, in the lowest quartile for gestational age

[¶]Vaso: treatment for hypotension with a vasopressor in the first 24 hours with any vasopressor (dopamine, dobutamine, and epinephrine)

[†]Labile: labile blood pressure, defined as the upper quartile of the difference in the lowest and highest MAP

VM= Moderate/Severe ventriculomegaly; EL=Echolucenct lesion

Q= Quadriparesis; D= Diparesis; H=Hemiparesis

PTL=Preterm labor; pPROM=Preterm premature rupture of fetal membranes

Table 3

Infant characteristics, indicators of hypotension, and indicators of white matter damage and cerebral palsy diagnosis (row percents).

Characteristics of the infant		Hypotension indicator			Indicators of white matter damage		Cerebral palsy			N
		Low Q[§]	Vaso[¶]	Labile[†]	VM	EL	Q	D	H	
Sex	Male	21	26	25	12	8	7	4	3	544
	Female	20	22	23	8	6	5	3	1	497
Type of gestation	Singleton	21	21	26	10	7	6	4	2	690
	Multiple	20	30	20	11	7	7	3	2	351
Gestational age (weeks)	23–24	19	35	28	14	10	13	8	3	209
	25–26	20	12	24	11	7	5	2	2	480
	27	24	20	21	7	5	3	3	1	352
Birth weight (grams)	≤ 750	20	29	28	11	7	9	5	3	383
	751–1000	23	23	23	8	7	4	2	2	458
	≥ 1000	18	18	18	13	9	6	4	1	200
BW Z-score*	< -2	25	21	32	7	2	2	0	5	56
	≥ -2, < -1	20	24	29	11	2	6	3	1	141
	≥ -1	21	24	22	7	8	6	4	2	844
HC Z-score*	< - 2	26	27	28	7	2	5	0	4	82
	≥ -2, < -1	21	21	24	8	6	6	5	1	234
	≥ -1	20	24	23	12	8	7	4	2	690
SNAP-II	< 20	13	16	21	7	6	5	2	1	536
	20–39	24	24	24	10	8	7	5	2	256
	≥ 30	35	44	31	17	8	9	6	3	232
Max number of infants		216	252	247	105	73	64	37	19	1041
Row percent		21	24	24	10	7	6	4	2	

[§]Low Q: lowest MAP recorded in the first 24 hours, in the lowest quartile for gestational age

[¶]Vaso: treatment for hypotension with a vasopressor in the first 24 hours with any vasopressor (dopamine, dobutamine, and epinephrine)

[†]Labile: labile blood pressure, defined as the upper quartile of the difference in the lowest and highest MAP

VM=Moderate/Severe ventriculomegaly; EL=Echolucenct lesion

Q=Quadriparesis; D= Diparesis; H=Hemiparesis

SNAP-II=Score for Neonatal Acute Physiology II

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Table 4

Frequencies of indicators of hypotension, and indicators of white matter damage and cerebral palsy diagnosis (row percents).

Exposures & outcomes		Lowest Q[§]	Vaso- pressor[¶]	Labile MAP[†]	Ultrasound		Cerebral palsy			N
					VM	EL	Q	D	H	
Lowest Q[§]	Yes		44	42	13	6	6	3	2	216
	No		19	19	9	7	6	4	2	825
Vasopressor[¶]	Yes	38		30	12	6	6	4	2	252
	No	15		22	10	7	6	4	2	789
Labile MAP[†]	Yes	37	31		10	7	7	3	1	247
	No	16	22		10	7	6	4	2	794
Ventriculo-megaly	Yes	26	29	23		28	28	9	9	105
	No	20	24	24		5	4	3	1	936
Echolucent lesion	Yes	18	22	25	40		33	7	12	73
	No	21	24	24	8		4	3	1	968
Quadriparesis	Yes	22	23	27	44	38		0	0	64
	No	21	24	24	8	5		4	2	977
Diparesis	Yes	19	24	22	24	14	0		0	37
	No	21	24	24	10	7	6		2	1004
Hemiparesis	Yes	26	26	16	47	47	0	0		19
	No	21	24	24	9	6	6	4		1022
Maximum N		216	252	247	105	73	64	37	19	1041
Row percent		21	24	24	10	7	6	4	2	

[§]Low Q: lowest MAP recorded in the first 24 hours, in the lowest quartile for gestational age

[¶]Vaso: treatment for hypotension with a vasopressor in the first 24 hours with any vasopressor (dopamine, dobutamine, and epinephrine)

[†]Labile: labile blood pressure, defined as the upper quartile of the difference in the lowest and highest MAP

VM= Moderate/Severe ventriculomegaly; EL=Echolucenct lesion

Q= Quadriparesis; D= Diparesis; H=Hemiparesis