A LUNG ULTRASOUND SEVERITY SCORE PREDICTS THE RESPONSE TO TREATMENT OF PATENT DUCTUS ARTERIOSUS IN PRETERM INFANTS

Afshar N, Louis D, Elsayed Y

Background: A lung ultrasound score has been described to predict degree of oxygenation and non-invasive ventilation failure in preterm infants but never been evaluated in preterm infants with hemodynamically significant patent ductus arteriosus (HSPDA).
Objective: To test the hypothesis that a lung ultrasound severity score (LUSsc) can predict the response to medical treatment of HSPDA.
Study design: We prospectively evaluated LUSsc that was conducted on preterm infants <30 weeks gestation with HSPDA at the time of assessment by targeted neonatal echocardiography (TNE), and repeated after confirmed closure or restriction of the ductal shunt after medical treatment. All ultrasound studies were done as per local protocol for assessment of 3 lung zones (upper, lower and lateral). Each zone was assessed for 4 different patterns and score (figure 1): Pattern 1: aerated lung with transverse repetition of artifact A-lines=0; pattern 2: separated longitudinal artifact B lines >2 in one frame representing interstitial edema=1; pattern 3: coalescent B lines representing alveolar edema=2; pattern 4: subpleural consolidation with air bronchograms=3, maximum score 18. A receiver operator curve was constructed to assess the ability to predict restriction of the ductal shunt after treatment.
Results: We studied 12 infants at median (IQR) gestation and birth weight of 26 weeks (27- 28) and 825 grams (707-915) respectively. Median (IQR) of age at the time of studies was 9(6-17) days. The LUSsc had a range from 0(low risk) to 18 (high risk). Median (IQR) of HSPDA size was 2.5 (1.9-3.2) mm before medical treatment by non-steroidal anti-inflammatory drugs. LUSsc had an area under the curve of 0.77 (95% CI 0.62-0.96, P < 0.05) for the ability to predict ductal restriction. A LUSsc cut-off of 10 has sensitivity and specificity of 83% and 61%, and positive and negative predictive values of 86% and 66%, respectively.
Conclusions: LUSsc can detect improved lung edema and predict restriction of HSPDA by medical treatment.

Figure 1: The 4 typical patterns of LUSsc

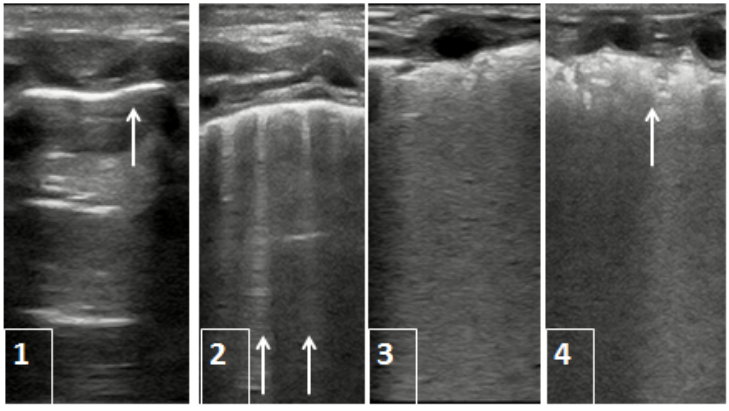

Table 1: Descriptive data of the studied groups presented as median (IQR) and percentages, p-value is bold when significant

	Before PDA treatment	After closure or constriction of PDA	P value
LUSsc	11 (12-13)	8 (7-12)	**<0.002**
Noninvasive ventilation	6 (50%)	9 (75%)	0.06
Mean airway pressure	9 (7-12)	9 (7-11)	0.4
Fraction of inspired oxygen	0.32 (0.25-0.37)	0.28 (0.23-0.33)	0.2
Left atrium :Aortic diameter ratio	2 (1.6-2.4)	1.4 (1.2-1.5)	**0.001**
Hemoglobin	130 (111-134)	114 (107-123)	0.4
PH	7.28 (7.24-7.33)	7.29 (7.27-7.41)	0.6
PaCO2	49 (39-57)	50 (41-59)	0.55
PaO2	40 (38-48)	48 (39-59)	0.09

INTEGRATED EVALUATION BY INTESTINAL ULTRASOUND AND NEAR INFRARED SPECTROSCOPY PREDICTS COMPROMISED INTESTINAL PERFORMANCE IN PRETERM INFANTS WITH FEEDING INTOLLERENCE

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Background: Feeding intolerance is a common problem in preterm infants, but the usefulness of integrated evaluation by intestinal ultrasound (IUS) and abdominal regional tissue oxygen saturation (RTO) in prediction of compromised intestinal performance (CIP) is novel and never been studied.

Objectives: The purpose of this study was to assess the value of using IUS and near infrared spectroscopy (NIRS) in predicting CIP in preterm infants with feeding intolerance.

Methods: Prospective study at 2 tertiary units in Winnipeg from 2016 to 2017 of 30 preterm infants, full assessment by IUS of 4 abdominal quadrants, and NIRS of right and left side of the abdomen by a trained physician was performed every 48 hours until establishment of full feeds.

Results: A total of 30 infants assessed at median (IQR) gestation and birth weight of 30 (31- 32) and 1908(1607- 2032) respectively, and underwent total of 82 assessments. 24 infants tolerated oral feeding as per unit protocol without interruption within the first 2 weeks of life, 6 infants developed clinical signs of feeding intolerance in the form of abdominal distention with recurrent emesis; and or bloody stools, only 2 of them radiologically diagnosed as necrotizing enterocolitis, but all of them showed at least 2 of the following sonographic abnormalities before development of the clinical signs of intolerance: hyperemia on color Doppler, sluggish peristalsis, intramural air, peritoneal fluid, non-collapsible dilated loops >0.5 cm, portal vein gases, and thinning of intestinal wall <0.11cm. Abdominal RTO was significantly lower for both left and right sides in infants with CIP.

Conclusions: Integrated evaluation by IUS and NIRS can predict CIP in preterm infants at least 48 hours before clinical signs of feeding intolerance, further studies are needed with management based on our approach.

Table 1: Descriptive data of the studied groups presented as median (IQR) and percentages, p-value is bold when significant

	Infants tolerated full feeds within 14 days N=24 (80%)	Infants with feeding intolerance N=6 (20%)	P value
Gestational age (weeks)	31(30-33)	29(28-32)	**<0.001**
Birth weight (grams)	2040(1767-2103)	1755(1502-2087)	**<0.001**
Male	16 (66%)	3 (50%)	0.07
Apgar at 5 min	9(8-9)	7(4-9)	**< 0.01**
Delayed cord clamping	14 (58%)	4 (66%)	0.6
Mechanical ventilation at time of assessment	5 (9%)	6 (23%)	**<0.05**
Age of first abnormal ultrasound (days)	-	4 (2-6)	-
Age of first sign of feeding intolerance (days)	-	9(4-14)	-
Age of established full feeding (days)	9(5-12)	19(15-23)	**<0.001**
Lactic acid (mmol/l)	1.8(1.2-2.3)	2(1.6-3)	**<0.05**
Intestinal wall diameter (cm)	0.2(0.18-0.22)	0.18(0.14-0.2)	**<0.001**
Right Abdominal RTO (%)	74(70-80)	69(64-75)	**<0.001**
Left Abdominal RTO (%)	75(70-81)	71(69-76)	**<0.001**

USE OF PULMONARY ARTERY DOPPLER WAVEFORM PARAMETERS IN ESTIMATING PULMONARY PRESSURES IN NEONATES

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Background: Estimation of pulmonary pressure is crucial in neonates with acute or chronic pulmonary hypertension. During echocardiography, the maximal velocity of the Tricuspid Regurgitant jet (TR Vmax) is usually used to estimate pulmonary pressures. However, TR jet can often be absent or unmeasurable in neonates, resulting in a need to search for alternative echocardiographic measures of pulmonary pressure.

Objectives: To identify the pulmonary artery doppler waveform parameter that most closely reflects pulmonary pressure in neonates and analyse the impact of baseline variables and measurement techniques on this relationship.

Methods: This was a retrospective cohort analysis conducted at two tertiary neonatal intensive care units. All neonates who underwent Targeted Neonatal Echocardiographic (TNE) assessments over the period of May 2014-May 2017 were assessed for eligibility. Neonates whose TNE revealed a complete TR jet were included. Echocardiographic parameters such as TR Vmax, Pulmonary artery doppler waveform parameters such as Right Ventricular Ejection Time (RVET) and Pulmonary Artery Acceleration Time (PAAT) were measured at main pulmonary artery level and the pulmonary valve level. Echocardiographic markers of right ventricular function, ductal and atrial shunts were recorded. Statistical analysis was performed using SPSS. Ethical approval was obtained from the institutional ethics board.

Results: 678 neonates with 1767 echocardiographic studies were screened for eligibility of which 201 scans were included. Mean gestational age of this cohort was 30.5+/-5.7 weeks. Pulmonary Vascular Resistance Index (PVRI), was calculated as ratio of RVET to PAAT. PVRI, measured by Pulsed Wave Doppler at the level of the main pulmonary artery was found to have the strongest correlation with RVSP estimated from TR Vmax. [$r=0.45$, $P<0.05$]. We could generate an equation to estimate systolic pulmonary artery pressures (ESPAP) directly from PVRI. [ESPAP= 25.53+3.97xPVRI, $p<.0001$]. At the multivariate level, systolic blood pressure at time of scan and PDA were found to have a statistically significance influence on this relationship.

Conclusion: PVRI, measured at the main pulmonary artery level had a statistically significant correlation with pulmonary pressures as measured by TR jet. Though, the strength of correlation is moderate at best and is influenced by presence of ductal shunt, it can still play an important role in assessment and monitoring of pulmonary pressures in neonates.

CARDIOVASCULAR DERANGEMENTS IN NEONATAL HERPES INFECTION

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Introduction: Disseminated Herpes Simplex Virus (HSV) infection is a severe neonatal illness. A significant proportion of affected neonates require intensive care support for circulatory insufficiency and hypoxic respiratory failure, with some even needing Extra Corporeal Membrane Oxygenation (ECMO). The pathophysiological contributors to the disease phenotype, the mechanisms underlying the hemodynamic instability and the best approach to treat such cardiovascular dysfunction have not been well described. Hence, we designed this study to identify patterns of cardiovascular dysfunction seen on Targeted Neonatal Echocardiographic (TNE) assessments in neonates with HSV infection and describe their response to physiology based hemodynamic management strategies.

Methods: A cohort of neonates with confirmed HSV infection admitted over the period of November 2014- April 2017 were included in this study. All neonates were evaluated by comprehensive TNE assessment within the first 24h of admission. Demographic and clinical data were collected retrospectively. All TNE measurements were performed by a single expert operator. Ethical approval was obtained from the institutional ethics board.

Results: Five neonates, 3 with HSV 1 and 2 with HSV 2, were identified during the study period. All had features of profound circulatory insufficiency such as hypotension, metabolic acidosis with high lactate, oliguria/anuria, poor capillary refill etc. Three neonates had severe oxygenation failure. On functional echocardiographic assessment, we found that all cases demonstrated underfilled cardiac chambers and low cardiac outputs suggesting severe vasodilatation and third space losses. These cases were managed by aggressive volume resuscitation and use of peripheral vasoconstrictors such as Vasopressin and Nor-Epinephrine. Primary ventricular dysfunction was identified in 3 neonates, who were treated with dobutamine and/or epinephrine. Significant pulmonary hypertension was detected in three infants which prompted the use of Inhaled Nitric Oxide. Acyclovir was initiated early on. Significant cardiovascular stabilization could be achieved by such targeted hemodynamic therapy. However, in view of extensive neurological and hepatic damage, life sustaining therapy was eventually withdrawn in all of them.

Conclusion: Hemodynamic instability in neonates with disseminated HSV infection may be related to either primary ventricular dysfunction, vasodilatation and third space losses or pulmonary hypertension. While, early TNE may enhance physiologic definition and facilitate targeted therapy, eventual prognosis remains poor and raises questions regarding utility of interventions such as ECMO.

NORADRENALINE IN PRETERM INFANTS WITH CARDIOVASCULAR COMPROMISE

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Introduction: Cardiovascular compromise is a frequent complication in preterm infants and associated with increased morbidity and mortality. Dopamine and Dobutamine are the most frequently used first line therapies. Noradrenaline (NA) is a naturally occurring sympathomimetic amine that acts on myocardial and vascular alpha and beta adrenergic receptors.NA is beneficial in the treatment of term newborns with cardiovascular compromise due to sepsis or pulmonary hypertension (PHN), but experiences with NA in preterm infants are limited.

Aim: The aim of this study is to review our clinical use of NA in preterm infants ≤ 32 weeks' gestation, and to describe its effectiveness and safety in this population.

Methods: This retrospective cohort study was undertaken at the Canberra Hospital, Canberra and John Hunter Children's Hospital, Newcastle. Neonates <= 32 weeks gestation born and received NA between 2004 to 2015 were included in the study. Patient records were reviewed for clinical data before and during NA use. We defined hypotension as a mean blood pressure (MBP) < infants post conceptional gestational age for more than 30 minutes, and a response to NA was determined when MBP reached above the gestational age in weeks of the neonate for at least 30 minutes. Side effects for NA were reviewed including tachycardia (>200), hypertension (SBP>90), liver and kidney injury. Long term follow-up was reviewed for neuro-developmental impairment.

Results: Forty-eight preterm infants received NA during the 11-year study period. Sepsis was the commonest cause of cardiovascular compromise followed by PHN. Median gestation was 27 weeks, weight was 952 grams. NA was used a first line inotrope in 5, second line in 15, 3rd line in 25 and as sole inotrope in 3 neonates. Details of NA use is shown in table 1. Effect of NA on cardiovascular factors and oxygenation is shown in table 2 and figure 1. Fifteen infants (31%) developed tachycardia. Twenty two (46%) of the 48 infants died. Follow up was available for 22 infants at 1 year. Four infants had mild and 5 had moderate to severe disability.

Conclusions: NA may be effective in treating preterm infants with hypotension associated with sepsis and pulmonary hypertension at relatively low doses and as first or second line inotrope. NA appears to be tolerated safely, however, mortality was high in this group of infants.

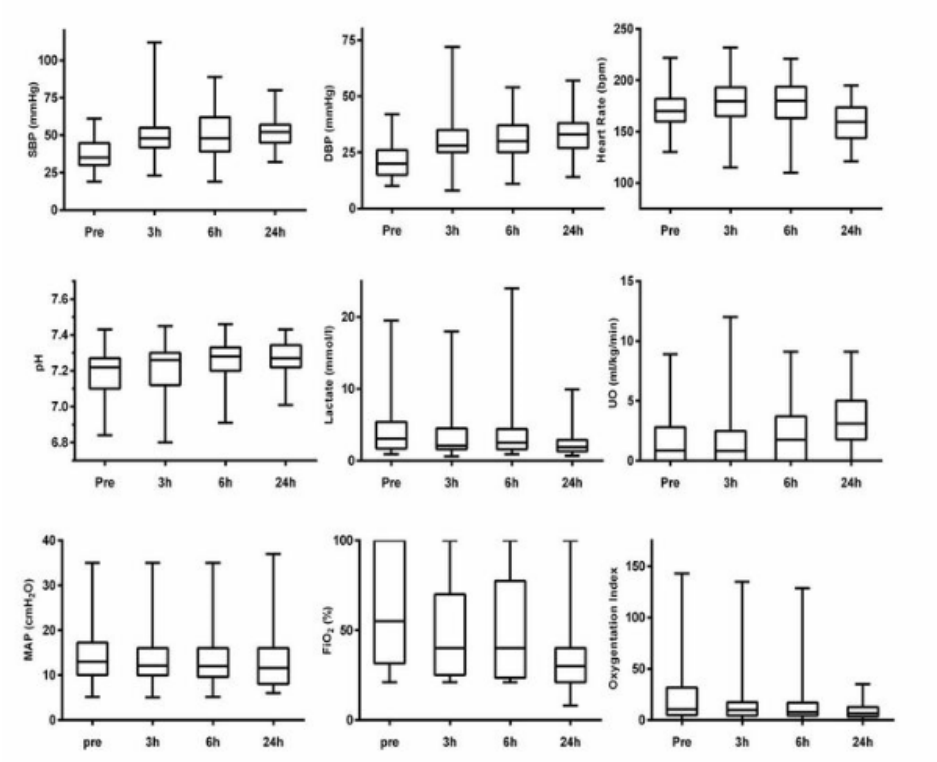
Table 1: Details of NA use in 48 preterm infants with cardiovascular compromise. Data presented as median (IQR)

Age at start NA (days)	1.5 (1-14)
Starting dose (mcg/kg/min)	0.4 (0.2-0.5)
Maximum dose (mcg/kg/min)	0.7 (0.4-1.0)
Dose at MBP restoration (mcg/kg/min)	0.5 (0.3-0.7)
Time to MBP restoration (hours)	1 (1-2)
Total duration of NA (hours)	29 (11-44)
Additional medications	
other inotropes	45 (94%)
Age at start NA (days)	19 (40%)
Starting dose (mcg/kg/min)	1 (2%)
Maximum dose (mcg/kg/min)	29 (60%)

Table 2: Median (IQR) of circulatory variables, blood gas variables and urine output before and 1 hour after normalisation of the mean blood pressure

Variable	before start of noradrenaline	1 hour after normalisation of MBP	p-value
SBP (mmHg)	34 (29-42)	44 (38-51)	<0.001
MBP (mmHg)	25 (22-30)	32 (29-39)	<0.001
DBP (mmHg)	20 (15-25)	26 (22-30)	<0.001
Heart Rate (bpm)	174 (161-185)	177 (164-199)	0.242
Mean Airway Pressure (cmH2O)	12 (9-15)	11 (10-16)	0.594
FiO2 (%)	45 (28-100)	37 (24-70)	0.043
Oxygenation Index	10 (5-24)	8 (4-15)	0.048
pO2 (mmHg)	52 (36-60)	54 (47-66)	0.109
Lactate (mmol/l)	3.4 (2-6)	2.3 (2-5)	0.146
pCO2 (mmHg)	53 (39-68)	49 (39-59)	0.109
pH	7.21 (7.11-7.28)	7.27 (7.19-7.30)	0.275
Urine output (ml/kg/hr)	0.6 (0.0-2.4)	1.7 (0.0-4.0)	0.113

Fig 1: Effect of noradrenaline on selected circulatory, perfusion and oxygenation parameters. The data is presented as median, IQR (box) and range (whiskers).



IMPACT OF ABNORMAL DIASTOLIC FLOW IN THE MIDDLE CEREBRAL ARTERY (MCA) ON NEURODEVELOPMENTAL OUTCOME OF PRETERM INFANTS WITH PERSISTENT EXPOSURE TO A HEMODYNAMICALLY SIGNIFICANT PATENT DUCTUS ARTERIOSUS (HSPDA)

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Background: Absent or reversed diastolic flow in the MCA has been reported in preterm neonates with hsPDA and influences clinical decision making. The clinical assumption is that abnormal diastolic flow in the MCA reflects a larger shunt as it represents preductal blood flow; hence, increased risk of abnormal neurodevelopmental outcome. Data regarding the clinical correlates of this finding are limited.

Objective: The goal of this study was to characterize the relationship between abnormal MCA diastolic flow and neonatal outcome in neonates with a persistent hsPDA.

Design/Methods: This was a retrospective cohort study of neonates with a PDA ≥ 1.5mm beyond day 14 of life, conducted at three tertiary neonatal intensive care units between June '11 - May '14. Comprehensive TnECHO evaluation of PDA shunt volume was routinely performed for all eligible patients. All echocardiograms were reviewed by a single trained expert and patients were classified based on exposure to absent/reversed (abnormal) or forward (normal) MCA diastolic flow. Blinding was ensured for assessment of MCA flow and neurodevelopmental outcome. The primary outcome was death or neurodevelopmental impairment (NDI) at 18-24 months, defined as a composite of moderate-severe neurosensory, neuromotor, and/or neurocognitive impairment assessed using the Bayley Scales of Infant Development-Third edition (BSID-III) and hearing/visual evaluation.

Results: 54 neonates were identified who satisfied eligibility criteria. There was no difference in baseline neonatal demographics between groups [Table 1]. Neonates with abnormal MCA flow were more likely to have abnormal celiac artery flow, demonstrated a trend towards lower peak systolic MCA velocity but other PDA characteristics were comparable. The frequency of PDA ligation was higher in patients with abnormal flow. There was no difference in the primary outcome between groups, although gross/fine motor scores were higher in the abnormal flow group [Table 2].

Conclusion(s): In neonates with persistent hsPDA greater than 14 days of life, abnormal MCA diastolic flow was not associated with increased risk of death or NDI at 18-24 months corrected gestational age. Given the unexpectedly high incidence of the primary outcome in this defined population, comparison with a matched cohort of neonates without a persistent hsPDA should be performed.

Table 1: Baseline characteristics and outcomes of preterm neonates with HSDA when categorized based on presence on presence of alternations in MCA diastolic flow.

Variable	Normal MCA flow (n=18)	Abnormal MCA flow (n=36)	P
GA (weeks) #	24.5 (24.2, 28.9)	25 (24.4, 26.8)	ns
BW (g)#	806 (683, 1159)	730 (625, 952)	ns
Female (n)‡	6 (33)	16 (44)	ns
Age at echo (days)*	21 (5)	22 (5)	ns
Echocardiography Characteristics			
HSDA size (mm) #	2.4 (2.0, 3.1)	2.3 (2.0, 2.4)	ns
Left ventricular output (ml/kg/min)*	386 (100)	403 (116)	ns
MCA systolic maximal velocity (m/s)*	0.55 (0.13)	0.49 (0.10)	0.06
Celiac artery systolic maximal velocity (m/s) #	0.64 (0.56, 0.7)	0.68 (0.56, 0.87)	ns
Therapy for HSDA			
Pharmacologic‡	16 (89)	28 (78)	ns
Ligation‡	1/17 (6)	12 (33)	0.04
Neonatal Morbidities			
Sensory-visual impairment‡	2/14 (14)	2/29 (7)	ns
Necrotizing enterocolitis‡	2 (11)	9 (25)	ns
Bronchopulmonary dysplasia at 36 weeks‡	8/17 (47)	22/30 (73)	ns
Intraventricular hemorrhage‡	11 (61)	25 (69)	ns
Periventricular leukomalacia‡	3 (17)	2 (6)	ns
‡frequency (percent); *mean (standard deviation); # median (IQR)			

Table 2: Outcomes of Preterms with HSDA and abnormal vs normal MCA diastolic flow

	Normal MCA flow (n=18)	Abnormal MCA flow (n=36)	P
Composite of death or abnormal Neurodevelopmental outcome‡	14 (78)	28 (78)	ns
Secondary Outcomes			
Death‡	1 (6)	6 (17)	ns
Cerebral palsy (CP) diagnosis‡	2/17 (12)	3/30 (10)	ns
Cognitive score*	85 (13)	91 (16)	ns
Composite gross/fine motor score#	80 (74, 84)	85 (82, 88)	0.01
Language score*	76 (15)	88 (20)	0.06
Sensory-visual impairment‡	2/14 (14)	2/29 (7)	ns
‡frequency (percent); *mean (standard deviation); # median (IQR)			

FEASIBILITY OF COMBINED MULTI-MODAL CEREBRAL MONITORING AND SERIAL HEMODYNAMIC ASSESSMENTS IN FIRST 72 HOURS OF LIFE IN EXTREMELY LOW GESTATIONAL AGE INFANTS

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Background: Extremely low gestational age (ELGA) infants represent a vulnerable population at high risk of acquired brain injury. Enhanced monitoring using cerebral near-infrared spectroscopy (NIRS), echocardiography and amplitude integrated electroencephalography (aEEG) may offer novel pathophysiological insights into precedents of brain injury. The feasibility of application of combined multimodal cerebral and hemodynamic monitoring in ELGA infants in clinical practice has not been tested.

Objective: The aim was to investigate the feasibility and safety of serial monitoring using combination of cerebral NIRS, aEEG, echocardiography, and head ultrasound in ELGA infants in the first 72 h after birth. Feasibility was defined a priori as 75% of the subjects satisfying at least 3 of the following 4 criteria: a) CrSO2 and b) aEEG monitoring each for > 75% of the time, c) at least 2 out of 4 echocardiograms and d) head ultrasounds (at least one by age 24 h).

Design/Methods: This prospective observational study was conducted at a tertiary NICU (Mount Sinai Hospital, Toronto). Infants born between gestational ages 23+0 and 27+6 weeks were included. Following parental consent, CrSO2 and aEEG monitoring was commenced by age 8 h and continued until 72 h. Sequential echocardiography and head ultrasound studies were performed at 4-8 h, 12-18 h, 24-30 h and 48-60 h.

Results: Of the 50 infants enrolled over 14 months, multimodal monitoring was feasible in 49 (98%) infants (Tables 1 & 2). Age at initiation and duration of monitoring (median and range) were 4.9 h (2.2-12) and 63 h (46.7-69.2) for CrSO2 and 5.5 h (2.9-12.5) and 64.6 h (34–68.7) for aEEG respectively. Mild self-limiting erythema lasting 3-8 h below CrSO2 sensors without skin breakdown was noted in 8/50 (16%). 23/50 (46%) infants had IVH (19 with Grade I/II and 4 with Grade III/IV). Drop in oxygen saturation (SaO2) was recorded during 17/199 (8.5%) ultrasound studies, the lowest SaO2 being 82%.

Conclusion: Multimodal monitoring is feasible, safe and well tolerated in ELGA infants in the first 72 h after birth. A larger study may help early identification of infants at risk of severe IVH.

Table 1: Demographics and perinatal characteristics

Clinical Characteristics	**N = 50**		
Female sex	20 (40%)		
Gestational age (weeks)	25.9 (23.1-27.9)		
Birth weight (g)	795 (500-1560)		
Inborn	49 (98%)		
Maternal age	31.34± 6.3		
Antenatal steroids	Complete: 38 (76%)	Incomplete: 7 (14%)	
Maternal chorioamnionitis	29 (58%)		
Perterm prolonged rupture of membranes	23 (46%)		
Intrapartum magnesium sulfate	38 (76%)		
Delayed cord clamping	28 (56%)		
Vaginal delivery	23 (46%)		
Apgar score 1 and 5 min	4 (0 – 9)	7 (1-10)	
Delivery room respiratory support	$^{\beta}$CPAP: 18 (36%)	$^{\gamma}$CMV 15 (30%)	$^{\delta}$HFO 17 (34%)
PPHN requiring iNO	4 (8%)		
Prophylactic indomethacin	21 (42%)		

Values are described as percentage, mean ± SD or median (range).*PPHN, Persistent pulmonary hypertension of the newborn; iNO, Inhaled Nitric oxide;CPAP, Continuous positive airway pressure; CMV, Conventional mechanical ventilation; HFO, High frequency oscillatio*

Table 2: Proportion of subjects fulfilling feasibility criteria, N=50

Modality criteria	N=50	Reason for exclusion from feasibility criteria
CrSO2> 75% in 72 h	46(92%)	N=4, loss of signal resulting in missing data
aEEG > 75% in 72 h	45(90%)	N=4, unavailability of aEEG equipment due to clinical requirement N=1, High impedance tracing
2/4 Echocardiograms, 1 within 24h	50 (100%)	-
4/4 Echocardiograms	49 (98%)	N=1, Research personnel not informed of birth[α]
2/4 Head Ultrasound, 1 within 24 h	50 (100%)	-
4/4 Head US	49 (98%)	N=1, Research personnel not informed of birth[α]
Subjects fulfilling 3/4 criteria	49 (98%)	N=1, aEEG and NIRS recorded< 75% time
Subjects fulfilling 4/4 criteria	41 (82%)	N=3, CrSO2 < 75% N=4, aEEG < 75% N=1, both aEEG and CrSO2 < 75% N=1, 3/4 Head ultrasounds and echocardiograms[α]

CrSO2, Cerebral oxygenation ; aEEG, Amplitude-integrated electro-encephalography [α]Same subject

PARACETAMOL FOR DUCTAL CLOSURE- AN EXPERIENCE FROM TERTIARY NEONATAL CENTRE IN SINGAPORE

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Introduction: Hemodynamically significant Patent Ductus Arteriosus (hsPDA) is associated with several complications in preterm neonates. The treatment and choice of agents has been a matter of debate due to serious side effects associated with these medications. Paracetamol as a drug to treat hsPDA with less serious side effects has been reported in several studies though the mode of administration, dose and duration varies. We present our experience with paracetamol for PDA closure in preterm neonates.

Aim: To study the efficacy of paracetamol in treating hsPDA.

Methods: Prospective observational study of paracetamol in preterm neonates with hsPDA for the duration of January 2016 to December 2017. All preterm babies treated with oral/intravenous paracetamol were included.

Results: Total 9 preterm babies with mean gestational age and birth weight of 26 weeks and 934 grams respectively received paracetamol therapy (Table 1). 8 (88%) babies had significant respiratory distress requiring assisted ventilation and surfactant therapy. Mean corrected gestational age at which paracetamol therapy initiated was 32 weeks. 7(77%) babies in the study population received at least one course of either indomethacin or ibuprofen prior to paracetamol therapy. The PDA size in study population varied from 2.2mm to 4.8mm, and all babies had continuous low velocity left to right shunt. 7 (77%) babies had significant left heart enlargement on echocardiography. The paracetamol dose used was 15mg/kg body weight for total of 20 doses administered over 5 days. Echocardiographic assessment post paracetamol treatment showed complete ductal closure in 1(11%) and reduction in ductal size in 4 (44%); one baby in this group needed PDA ligation. The ductal size remained unchanged in 4/9 (44%) and 2 babies in this group needed PDA ligation. Except for rebound unconjugated hyperbilirubinemia in one baby there were no significant adverse effects reported following paracetamol therapy.

Conclusion: In our study 3(33%) babies had favourable response following paracetamol therapy. This study adds that paracetamol was less effective in closing the duct, and reduction of ductal size observed in some neonates. A Larger randomized control studies are necessary in understanding the optimal dose, route and duration of administration for maximal clinical benefit.

Table 1. Baseline and Echocardiographic characteristics of study population

S. no	Birth Weight (grams)	Gestation at birth (weeks)	Sex	Corrected GA at Paracetamol Therapy	Previous failed Medical Therapy	Echocardiographic parameters			PDA ligation	Final outcome
						LA dilatation	PDA size	PDA shunt		
1	700	24+5	F	27+5	No	Yes	2.5mm	L to R	No	closed
2	1018	29+4	M	33+4	Yes (1 course)	Yes	4.2mm	L to R	No	Decreased size
3	530	25+4	M	33+2	Yes (1 course)	No	2.2mm	L to R	No	No change
4	1530	29+5	M	34+3	Yes (1 course)	Yes	2.3mm	L to R	No	Decreased size
5	580	24+2	F	27+3	Yes (1 course)	Yes	2.9mm	L to R	Yes	No change
6	670	24	M	37	Yes (1 course)	No	4.8mm	L to R	Yes	Decreased size
7	810	25	F	31	Yes (1 course)	Yes	2.8mm	L to R	No	Decreased size
8	955	26+5	M	34	Yes (1 course)	Yes	3mm	L to R	Yes	No change
9	1630	30+3	F	35	No	Yes	3.1mm	L to R	No	No change

DEXMEDETOMIDINE DOES NOT DECREASE BENZODIAZEPINE EXPOSURE FOR NEONATES AFTER CARDIAC SURGERY

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Introduction: In recent years, early tracheal extubation and fast-track postoperative care after congenital heart surgery has gained increasing support. Dexmedetomidine (Dex) is a selective [alpha]2-adrenoreceptor agonist, resulting in sedation, anxiolysis, and analgesia coupled with minimal concern for respiratory depression. It has been shown to be safe after surgery in neonates. We hypothesize that use of dexmedetomidine may offer benzodiazepine and opioid sparing effects for neonates for the first 48 hours after cardiac surgery.

Methods: All neonatal cardiac surgical patients admitted to CVICU from 1/2011 to 6/2015 ±cardiopulmonary bypass (CPB) were included. Every dose of opioid and benzodiazepine received via bolus or continuous infusion within first 48 hours post-operatively was counted; with cumulative doses converted to equivalents. We then compared neonates who received dexmedetomidine for sedation (DEX+) with those who did not (DEX-). Only the index surgery was included and those treated with ECMO were excluded. Wilcoxon rank-sum test, Fisher's exact test and multiple linear regression analysis were used as appropriate to compare outcomes for DEX+ versus DEX- . We set the p value at <0.05.

Results: There were 359 neonates who had cardiac surgery in the time period, 92 of which were in the Dex+ group and 267 in the Dex- group. The groups were similar in demographics, although the Dex + newborns were predominantly male ($p<0.001$) and had higher mean weight ($p=0.003$), the groups were not significantly different in terms of Stat 1-3 vs STAT 4&5 ($p=0.077$), use of CPB ($p= 0.181$) or prematurity ($p=0.265$). Total benzo dose in the first 48 hours post-operatively was not significantly different between the DEX + vs DEX -group ($p=0.274$). Total opioid in morphine equivalents per kilogram (ME) was significantly higher ($p<0.001$) in DEX+ compared to DEX- . Length of stay was marginally higher in the DEX group ($p=0.077$). In multi-variate analysis, total ME Dose remained higher for patients receiving DEX ($p=0.004$), but total Benzos dose was not significantly different for the DEX+ versus DEX- group ($p=0.375$).

Conclusion: Dexmedetomidine infusion in the first 48 hours after cardiac surgery in neonates may not limit the exposure to benzodiazepines as previously thought. Even when controlling for other variables, those newborns receiving DEX were found to have an association with higher opioid exposure.

TARGETED NEONATAL ECHOCARDIOGRAPHY (TNECHO) IN THE NEONATAL INTENSIVE CARE UNIT: 1-YEAR EXPERIENCE IN A TERTIARY LEVEL UNIT IN MEXICO CITY

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Background: Focused assessment of myocardial performance and hemodynamics directed by a clinical question performed by a neonatologist has demonstrated on several retrospective studies to guide and modify management in neonatal intensive care units (NICU). The TnECHO program in Mexico City started on January 2017 after one of the physicians of the team completed the advanced fellowship training in the Canadian program.

Objective: To evaluate the impact of a TnECHO program within one year of its institution on a tertiary level NICU in Mexico City.

Design/Methods: A database containing demographic information, indication for TnECHO, hemodynamic variables, and change in management after the consult was collected during 2017.

Results: 158 studies were performed on 69 patients (4 excluded for mayor congenital heart disease). Indication for the consults were acute pulmonary hypertension (aPH) in 63 (40%), patent ductus arteriosus (PDA) in 42 (27%), systemic hemodynamics in 26 (16%), pulmonary hemodynamics/chronic pulmonary hypertension assessment in 24 (16%) and thrombus/vegetation's surveillance in 3 (2%). [Table 1]. 85 consults resulted in change in management (54%). 28 consults (18%) presented unexpected findings (malpositioned catheter tips, intracardiac thrombus, minor structural heart disease). [Table 2].

Conclusions: TnECHO program is a valuable tool for hemodynamic assessment leading to an active change in management in 54% of the consults. Carefully designed studies should be done in the future assessing the impact of TnECHO on neonatal outcomes.

Table 1: Frequency and percentage in management change between common hemodynamic conditions.

	Frequency	Percent (%)
aPH (N 63)		
Pulmonary vasodilator therapy	18	28
Escalation of pulmonary vasodilators	1	2
De-escalation of pulmonary vasodilators	4	6
Systemic vasopressor initiation	7	11
Change in systemic vasopressors	1	2
De-escalation of systemic vasopressors	3	5
Prostaglandin infusion	1	2
Total change	35	56
PDA (N 42)		
Conservative to medical	10	24
Medical to conservative	4	10
Medical to surgical	3	7
Surgery avoidance	1	2
Total change	18	43
Systemic hemodynamics (N 26)		
Avoidance of medical therapy	5	19
Inotrope and/or vasopressor initiation	7	27
Escalation of inotrope and/or vasopressor	3	11.5
Change in choice of inotrope and/or vasopressor	1	4
De-escalation of inotrope and/or vasopressor	3	11.5
Total change	19	73
Pulmonary hemodynamics/ chronic pulmonary hypertension (N 24)		
Diuretics for chronic pulmonary hypertension RV dilation	8	33
Diuretics for PFO/ASD	3	13
Total change	11	46

EFFECT OF HEMODYNAMICALLY SIGNIFICANT DUCTUS ARTERIOSUS ON DOPPLER FLOW PATTERNS OF PULMONARY VEINS IN PRETERM INFANTS

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Background: The assignment of hemodynamic significance to a patent ductus remains a challenge for neonatal intensivists. Comprehensive echocardiography evaluation is warranted to assess not only ductal size but shunt volume. Many parameters, used to adjudicate hemodynamic significance, are fraught with poor sensitivity and specificity.
Objective: To assess the utility of Doppler flow patterns of pulmonary veins in preterm infants with hemodynamically significant ductus arteriosus (hsDA) requiring medical therapy and/or ligation in comparison to those without a patent ductus arteriosus (PDA).
Methods: A retrospective chart review of preterm infants evaluated for an hsDA, between August 2011 to December 2014 at 2 tertiary centers, was performed. The infants were categorized in 3 groups: Group 1 (No evidence of a PDA), Group 2 (hsDA requiring medical therapy only) and Group 3 (hsDA requiring surgical ligation). Intergroup comparison was performed using ANOVA and non-parametric methods.
Results: 144 preterm infants [group 1 (n=45), group 2 (n=79) and group 3 (n=20)] were studied. Baseline characteristics between the three groups were similar. Infants with HSDA requiring either medical therapy or surgical ligation had higher pulmonary vein D wave Doppler and lower pulmonary vein S/D ratio in comparison to infants with no PDA (Table 1). Infants with hsDA undergoing ligation had a statistically significant high pulmonary vein D wave Doppler versus those who received medical therapy but no significant difference with regards to pulmonary vein S/D ratio.
Conclusions: Pulmonary vein Doppler could be a simple and useful aid in adjudicating hemodynamic significance for ductus in preterm infants.

Table 1: Comparison of Doppler waveforms amongst preterm infants with or with no HSDA

Pulmonary vein Doppler	Group 1 (n=45)	Group 2 (n=79)	Group 3 (n=20)	P value
D wave (cm/s)	31.39(0.07)	41.33(0.11)	54.7(0.28)	< 0.0001
S/D ratio	1.17(0.22)	0.94(0.21)	0.87(0.24)	< 0.0001
LVO (ml/kg/min)	251.7(57.39)	327.9(105.93)	402.4(122.05)	<0.0001
DA diameter (mm)	-	2.21(0.69)	2.09(0.55)	0.47

Values expressed as mean $\pm$ S.D.

HIGH DOSE VERSUS STANDARD DOSE IBUPROFEN FOR PATENT DUCTUS ARTERIOSUS IN PRETERM INFANTS –A META-ANALYSIS

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Background: Observational studies have suggested that high dose ibuprofen may be an alternative to standard dose ibuprofen for the closure of a hemodynamically significant ductus arteriosus (hsDA) in preterm infants. To determine the efficacy and safety of high dose ibuprofen compared with standard dose ibuprofen (10,5,5mg/kg/d) for closure of a hsDA in preterm infants.

Methods: We conducted searches of the Cochrane Central Register of Controlled Trials (CENTRAL, Cochrane Library), MEDLINE, EMBASE and CINAHL in March 2018. We identified two randomised controlled trials (RCTs) and three observational studies that compared high dose to standard dose ibuprofen for the treatment of an echocardiographically diagnosed hsDA in preterm infants. Primary outcome was failure of ductal closure after first course of ibuprofen treatment. Secondary outcomes were rates of renal insufficiency, oliguria, hyperbilirubinemia, thrombocytopenia, NEC, sepsis, IVH, mortality, duration of hospital stay and levels of serum creatinine, bilirubin, platelets post treatment.

Results: Two RCTs and three observational studies comparing high dose versus standard dose ibuprofen for treatment of hsDA that enrolled 309 infants were included. There was significant difference between treatment with high dose versus standard dose ibuprofen favouring high dose ibuprofen for failure of ductal closure after the first course of drug administration (typical relative risk (RR) 0.64, 95% confidence interval (CI) 0.47 to 0.87; NNTB 6, typical RD -0.15, 95% CI -0.25 to -0.05; I2 = 59% for RR and I2 = 38% for RD). On sensitivity analysis after exclusion of observational studies, there was significant difference between treatment with high dose versus standard dose ibuprofen favouring high dose ibuprofen for failure of ductal closure after the first course of drug administration (typical relative risk (RR) 0.27, 95% confidence interval (CI) 0.11 to 0.64; NNTB 4, typical RD -0.23, 95% CI -0.36 to -0.10; I2 = 35% for RR and I2 = 0% for RD). There were no significant differences between the paracetamol and the ibuprofen groups with regards to secondary outcomes.

Conclusions: In comparison to standard dose ibuprofen, high dose ibuprofen appears to be more effective and safe in closure of hsDA in preterm infants.

PARACETAMOL FOR PATENT DUCTUS ARTERIOSUS IN PRETERM INFANTS –A META-ANALYSIS

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Background: Case reports and few trials have suggested that paracetamol may be an alternative for the closure of a hemodynamically significant ductus arteriosus (hsDA). To determine the efficacy and safety of intravenous or oral paracetamol compared with placebo or no intervention, intravenous (iv) indomethacin, iv or oral ibuprofen, for closure of a hsDA in preterm infants.

Methods: We conducted searches of the Cochrane Central Register of Controlled Trials (CENTRAL, Cochrane Library), MEDLINE, EMBASE and CINAHL for articles quoting identified randomised controlled trials. All searches were conducted in March 2018. We identified five randomised controlled trials (RCTs) that compared oral paracetamol to oral ibuprofen, one RCT that compared iv paracetamol to iv ibuprofen and iv indomethacin, one RCT that compared oral paracetamol to iv indomethacin for the treatment of an echocardiographically diagnosed hsDA in preterm infants. In addition, one RCT compared prophylactic iv paracetamol to placebo.

Results: Six RCTs comparing oral/iv ibuprofen versus oral/iv paracetamol for treatment of hsDA that enrolled 688 infants were included. There was no significant difference between treatment with oral/iv paracetamol versus oral/iv ibuprofen for failure of ductal closure after the first course of drug administration (typical relative risk (RR) 0.90, 95% confidence interval (CI) 0.71 to 1.13; typical RD -0.03, 95% CI -0.10 to 0.04; I2 = 0% for RR and I2 = 0% for RD).There were no significant differences between the paracetamol and the ibuprofen groups in the secondary outcomes except for gastrointestinal bleeding (typical RR 0.28, 95% CI 0.12 to 0.69, NNTB 17, n = 4 studies, n = 537 infants), for serum creatinine levels (MD-0.09 mg/dl, 95% CI -0.12 to -0.07; I2 = 88%, n= 537 (4 studies)) and for serum bilirubin levels post treatment (MD – 11.25 mmol/L, 95% CI -13.88 to -8.62; I2 = 39% for WMD, n= 290 infants (2 studies)) in favour of paracetamol. 1 RCT reported neurodevelopmental outcomes at 18-24 months and found no significant difference in neurodevelopmental outcomes between the two groups. Two RCTs comparing iv indomethacin versus oral/iv paracetamol for treatment of hsDA that enrolled 273 infants were included. There was no significant difference between treatment with oral/iv paracetamol versus iv indomethacin for failure of ductal closure after the first course of drug administration (RR 0.96, 95% CI 0.55 to 1.65; typical RD -0.01, 95% CI -0.09 to 0.08; I2 = 11% for RR and I2 = 17% for RD). There were no significant differences between the paracetamol and the ibuprofen groups in the secondary outcomes except for serum creatinine levels post treatment (MD -0.35 mg/dl, 95% CI -0.39 to -0.31, n=200 (1 study)). With regards to prophylactic paracetamol versus placebo, one RCT concluded that the ductus closed faster in the paracetamol group (hazard ratio 0.49, 95% CI 0.25-0.97, P = .016) without any adverse effects.

Conclusions: Oral or iv paracetamol appears to be as effective in closing a PDA as oral/iv ibuprofen or iv indomethacin with a better adverse effect profile with limited long term neurodevelopmental follow up data available.

CLINICAL BURDEN OF POSTNATALLY ACQUIRED ACUTE CARDIOPULMONARY CRITICAL ILLNESS AMONG PRETERM NEONATES OF <32 WEEKS GA

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Background: Despite being a frequently encountered complication in contemporary neonatal practice and a major cause of mortality, postnatally acquired acute cardiopulmonary critical illnesses (CCIs) affecting premature neonates have rarely been a subject of research.
Objective: To assess the disease burden associated with CCIs, as identified by significant exposure to treatment with inotropes and/or inhaled nitric oxide (iNO), in preterm neonates admitted to tertiary NICUs in Canada, and to determine factors associated with mortality.
Design/Methods: A retrospective cohort study was performed using the Canadian Neonatal Network (CNN) database, including preterm infants of ≤ 32 weeks gestational age (GA) admitted to tertiary Canadian NICUs between 2010 and 2016. CCI was defined as any of the following exposures occurring after 3 days of age: 1) inotrope or iNO for ≥ 3 consecutive days; 2) inotrope and iNO for ≥ 2 consecutive days; 3) inotropes or iNO within 2 days before death. Comparison was performed between survivors versus those who died. Multivariable analysis (MVA) was performed to identify factors associated with mortality in CCIs. Inter-site variability in the incidence of CCIs and associated mortality was also examined. A subgroup analysis was performed for those with CCIs secondary to culture-positive sepsis.
Results: The incidence of CCIs in the study population was 7.6% (n=2175), with a mortality rate among CCI neonates of 42% (n=917). Important differences were observed between neonates who survived versus those who died (Table 1). MVA revealed higher GA at birth [adjusted odds ratio (95% confidence interval) 0.93 (0.89, 0.97)], greater postnatal age at
CCI [0.98 (0.97, 0.98)], use of antenatal steroid [0.69 (0.52, 0.91)] and postnatal surfactant [0.74 (0.56, 0.99)] to be favorable factors, while prior diagnosis of sepsis [1.54 (1.24, 1.90)] or NEC [3.55 (2.72, 4.63)] was adversely associated with mortality. Significant inter-site variability was observed in both the incidence of CCIs as well as associated mortality ($p<0.01$; Figure 1). Irrespective of the identification criteria, CCI survivors demonstrated a high rate of common neonatal morbidities. Restricting the analysis to neonates with sepsis revealed similar
results.
Conclusion: CCIs affect a significant number of preterm neonates. The associated high mortality and morbidity as well as significant inter-site variability support an urgent need for focused research and specific quality improvement initiatives for improving outcomes in this specific population.

SERUM CORTISOL LEVELS IN ASPHYXIATED INFANTS WITH HYPOTENSION

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Background: Hemodynamic instability due to cardiovascular insufficiency is a common complication in asphyxiated, cooled neonates. Hypotension is often resistant to volume and catecholamine administration, which could be related to low serum cortisol values. Relative adrenal insufficiency (RAI) has not been studied in detail in critically ill, hypotensive neonates with perinatal asphyxia between the 0-168th postnatal hours (during and immediately after hypothermia treatment).
Aims: To assess serum cortisol values in asphyxiated, hypotensive infants treated with hypothermia and examine the relationship between serum cortisol values and severity of illness.
Methods: We conducted a retrospective cohort study between 2007-2016, including term neonates with moderate-to-severe hypoxic-ischemic encephalopathy who underwent standard hypothermia treatment. Cortisol values were measured in 79 infants whenever hypotension occurred in the first week of life.
Results: Serum cortisol values displayed an exponential decay characteristic after birth with 89% of the measurements being less than 15 μg/dl, the threshold of RAI. Infants with more severe condition measured on the SNAP-II scale had significantly higher cortisol values during hypothermia (moderate-severe 5.0 [3.9;10.9] μg/dl vs mild condition 2.8 [2.0;4.6] μg/dl; p=0.002). Eventually 57% of patients received low-dose hydrocortisone supplementation (HCS) at a median dose of 0.6 [0.5;1.0] mg/kg due to hemodynamic instability and suspected RAI. Among those who were available for follow-up, patients with or without HCS scored similarly on the Bayley-II.
Conclusions: Our results suggest that asphyxiated, cooled infants presenting with hypotension were likely to have low serum cortisol values. Further studies are needed to test the efficacy and long-term safety of hydrocortisone administration in the treatment of hypotension in asphyxiated, cooled neonates.

HYDROCORTISONE TREATMENT IN SYSTEMIC LOW BLOOD PRESSURE DURING HYPOTHERMIA IN ASPHYXIATED NEWBORNS (CORTISoL trial)

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Background: Asphyxiated neonates frequently present with haemodynamic instability, or volume and catecholamine resistant hypotension. Relative adrenal insufficiency (RAI) could be considered as an underlying etiology, and hydrocortisone treatment may be a causative therapy in selected infants. To date, hydrocortisone treatment for systemic hypotension in infants with hypoxic-ischemic encephalopathy (HIE) undergoing hypothermia has not been formally evaluated.
Methods: A double-blind, randomized, placebo-controlled clinical trial was conducted in the NICU of the 1st Department of Paediatrics, Semmelweis University between 2016 and 2017 (ClinicalTrials.gov identifier: NCT02700828). Thirty-five HIE neonates with systemic low blood pressure during hypothermia treatment were randomly assigned to receive 0.5 mg/kg/6 hours hydrocortisone or placebo beside standard dopamine treatment. Primary outcome was the change in mean arterial blood pressure in the patients receiving hydrocortisone vs placebo.
Results: The baseline clinical characteristics were similar between the study groups. Serum cortisol concentrations were low immediately before randomization both in hydrocortisone and placebo groups, suggesting the presence of RAI. Significantly more HIE infants treated with hydrocortisone reached 5 mmHg increase in mean arterial blood pressure at the 2nd hour after the initiation of intervention compared to controls (94% vs 63%, respectively, p=0.033). Furthermore, patients with hydrocortisone treatment received significantly less vasopressor-inotropic support as measured by the duration and cumulative dose of catecholamines compared to controls (median 47 [18;78] vs 92 [70;102] hours, p=0.005; and median 10 [3;27] vs 51 [27;57] mg/kg, p=0.001, respectively). Results of the long-term follow-up examinations on the Bayley-II neurodevelopmental test are still being evaluated.
Conclusion: Our results suggests that hydrocortisone administration was effective in raising the blood pressure and decreasing the catecholamine need of HIE patients with hypotension during hypothermia. Data regarding the long-term safety of hydrocortisone treatment is still awaited in this population.

ASSOCIATION BETWEEN CLINICAL FACTORS RELATED TO LATE-ONSET CIRCULATORY COLLAPSE AND BRAIN DAMAGE IN PRETERM INFANTS

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Objective: Late-onset circulatory collapse (LCC) has been reported that premature babies of more than 7 days old develop circulatory failure in response to glucocorticoid therapy. The aim of this study is to identify clinical factors that increase brain damage in LCC patients.

Methods: We retrospectively reviewed total of 167 preterm infants who were born at <35weeks gestation and had hypotension between Apr. 2009 and Mar. 2017 at SMG-SNU Boramae Medical Center. Patients with cardiac diseases including patent ductus arteriosus, confirmed infection, massive hemorrhage, pneumothorax, or congenital anomaly were excluded. Forty infants with hypotension and oliguria after 7days were classified to LCC. We divided the patients into two groups based on ultrasonography and magnetic resonance imaging results; infants with periventricular leukomalacia (n=9) and normal image (n=31) after LCC. The clinical factors including perinatal characteristics, clinical features at LCC period and neonatal morbidities of these two groups were compared.

Results: The incidence of LCC was 6% (n=40) and the distribution showed highest at gestational age of 26 weeks (29%) and body weight of 1001-1250g (22%). The incidence of brain damage in LCC patients was 23% (n=9). There was no significant difference in perinatal characteristics and postnatal morbidities between two groups according to brain damage. Postnatal age (PNA) was older in the group with brain damage (16 vs 24 days, p=0.047). The lowest mean blood pressure (MBP) and the lowest serum sodium concentration were significantly lower in the brain damage group (19 vs 22 mmHg, p=0.034; 125 vs 129 meq/L, p=0.043). There was no significant difference in hypotension duration, oliguria, the highest potassium concentration, cortisol level, inotropic use, hydrocortisone initiation time and duration of the treatment between two groups. In receiver-operating characteristic curve for predictors of brain damage in LCC infants, the cut-off values of PNA, MBP, and sodium concentration were 20 days (sensitivity=0.556, specificity=0.677), 20.5 mmHg (sensitivity=0.667, specificity=0.581), and 127.5 meq/L (sensitivity=0.667, specificity=0.677), respectively.

Conclusion: Infants with lower serum sodium level and lower MBP during LCC period had more brain damage. Therefore, fast initiation of hydrocortisone and management for normalizing the serum sodium level and MBP are important in LCC patients.

VALIDATION OF RIGHT VENTRICULAR OUTPUT CALCULATION IN A COHORT OF HEALTHY NEONATES

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Background: Right ventricular output (RVO) is routinely used to asses right ventricular (RV) systolic performance to guide clinical decision making. It is possible to image the right ventricular outflow tract and estimate RVO from different imaging planes, but the reliability and precision of each technique is unknown. In patients with no intracardiac shunt or patent ductus arteriosus, RVO should approximate left ventricular output (LVO).
Objective: The aim of this study was to characterize the reliability and accuracy of RVO calculation from three standardized echocardiography imaging planes.
Design/Methods: To validate RVO, echocardiograms were considered eligible if comprehensive right heart function assessment was performed and all imaging planes were available for analysis, there was no evidence of patent ductus arteriosus or atrial septal defect, and myocardial function was normal. Components of RVO [velocity time integral (VTI, pulsed wave Doppler), heart rate (HR), pulmonary artery (PA) annulus diameter (2D)] were measured by a single operator in 3 imaging planes [parasternal long axis (PLx), parasternal short axis (PSx) and apical RV 3 chamber (RV3)]. Components of left ventiricular output (LVO) were measured from an apical 5-chamber view. The average of 3-5 readings was obtained for each measurement. Outputs were calculated according to the formula [HR*VTI*πr2]/weight. Agreement was determined by calculating median bias for each imaging plane in relation to LVO using Bland-Altman analysis and Spearman correlation coefficients. Concordance within/between observers was assessed using intra-class coefficient (ICC) and coefficient of variation (COV) in a subset of 15 echocardiograms.
Results: RVO calculated from all imaging planes showed significant agreement with LVO. [Table 1] RV3 chamber view showed the lowest median bias [-6mls/kg/min] and highest correlation co-efficient [0.71, p<.001]. Intra-observer ICC was >0.96 for RV VTI and PA diameter, regardless of imaging plane. The highest inter-observer agreement for RV VTI [ICC 0.94 (0.86, 0.97)] and PA diameter [ICC = 0.84 (0.65, 0.93)] was from the PSx plane.
Conclusion(s): RVO may be calculated from different imaging planes with acceptable bias and low intra/interobserver variability. Although RV3/PSx imaging planes showed the lowest median bias and interobserver variability, the optimal method used clinically to estimate RVO should be based on the quality of the imaging plane and the standardization of measurement techniques.
Conclusion: RVO calculated from 3 different imaging planes showed excellent agreement with low bias and low intra/inter-observer variability. RV3/PSx planes showed the lowest bias and inter-observer variability. The optimal method used clinically to estimate RVO should be based on the quality of the imaging plane and the standardization of measurement techniques.

Imaging plane	RVO [ml/min/kg]	Median Bias [95% CI]	Spearman coefficient
RV 3 Chamber	241 (105, 579)	-6.23 (-27.0, 7.00)	0.71 (p < .0001)
Parasternal short axis	269 (72.0, 855)	-12.09 (-26.0, 1.00)	0.70 (p < .0001)
Parasternal long axis	264 (84.0, 720)	-9.66 (-32.0, 5.00)	0.61 (p < .0001)
LVO [ml/min/kg]	227 (142, 502)	-	1.00000

	Intra-observer (1 & 2)		Inter-observer (1&3)	
	ICC* (95% CI)	BA 95% LOA	ICC (95% CI)	BA 95% LOA
PA-VTI-3C	0.965 (0.905, 0.983)	-0.45, 0.20	0.80 (0.57, 0.91)	-1.27, 0.16
PA-VTI-SAX	0.977 (0.952, 0.992)	-0.46, 0.09	0.94 (0.86, 0.97)	-0.64, 0.24
PA-VTI-LAX	0.986 (0.976, 0.996)	-0.37, 0.13	0.94 (0.86, 0.97)	-0.51, 0.05
PA-DIAM-3C	0.989 (0.976, 0.996)	-0.01, -0.002	0.83 (0.63, 0.93)	-0.02, 0.03
PA-DIAM-SAX	0.984 (0.952, 0.992)	-0.01, 0.004	0.84 (0.65, 0.93)	-0.001, 0.05
PA-DIAM-LAX	0.989 (0.976, 0.996)	-0.01, 0.01	0.83 (0.63, 0.93)	-0.004, 0.04
AO-VTI	0.974 (0.927, 0.989)	-0.18, 0.38	0.94 (0.86, 0.97)	-0.58, 0.27
AO-DIAM	0.987 (0.976, 0.996)	-0.01, -0.003	0.85 (0.67, 0.94)	-0.03, 0.01

ECHOCARDIOGRAPHY FEATURES OF INFANT OF DIABETIC MOTHER AS COMPARED TO HEALTHY FULL-TERM CONTROLS

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Introduction: M-mode and 2-D echocardiography can show asymmetric septal hypertrophy and fetal ventricular walls thickness that simulates idiopathic hypertrophic subaortic stenosis which increases progressively with advancing gestation.

Aim: To compare echocardiographic findings of infants of diabetic mothers (IDMs) and healthy full term appropriate for gestational-age (AGA) infants of nondiabetic mothers.

Methods: The study was done as a case–control study included a group of 58 IDMs and 60 healthy AGA neonates over a period of one year. A Sonosite Edge ultrasound with an 8 MHz transducer was used to measure echocardiographic parameters. Baseline characteristics and outcome measures on continuous scales were analysed by using two sample t test or Mann Whitney U test as appropriate. Statistical significance was considered if the p-value was <0.05.

Results: The inter-ventricular septal (IVS) thickness was significant in cases vs control [at end systole 5.2 mm (Q1 4.4, Q3 5.58) = vs. 4.9 mm (Q1 4.5, Q3 5.23), p=0.045; at end diastole = 4.85 mm (Q1 4.0, Q3 5.0) vs. 4.4 mm (Q1 3.9, Q3 4.8), p=0.017]. The IVS/LVPW ratio was not significantly higher in IDM than controls [median 1.09 (Q1 0.97, Q3 1.16) vs 1.02 (Q1 0.97, Q3 1.06) p= 0.51] but was significant when HBA1C was >6.5% vs <6.5% [median 1.21 (Q1 1.04, Q3 1.44) vs 1.04 (Q1 0.96, Q3 1.125) p= 0.003] End point septal shortening(EPSS) a major of diastolic function was significantly low in IDMs than control [median 2.5mm (Q1 1.6, Q3 3.0) vs 3.2 (Q1 2.6, Q3 3.7) p <0.0001] 4 babies who required respiratory support and propranolol had IVS/LVPW >1.5 and EPSS <1.0mm, out of which two babies expired.

Conclusions: The present study suggests that IVS/LVPW and EPSS can be used as a marker which babies might require early intervention.