www.jpnim.com Open Access eISSN: 2281-0692
Journal of Pediatric and Neonatal Individualized Medicine 2015;4(2):e040207
doi: 10.7363/040207
Published online: 2015 Sept 08

Abstracts

Selected Abstracts of the 1st Congress of joint European Neonatal Societies (jENS 2015) · Session "Circulation, O_2 Transport and Haematology"

BUDAPEST (HUNGARY) · SEPTEMBER 16TH-20TH 2015

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[Abstract's authors]. [Abstract's title]. In: Selected Abstracts of the 1st Congress of joint European Neonatal Societies (jENS 2015); Budapest (Hungary); September 16-20, 2015; Session "Circulation, O_2 Transport and Haematology". J Pediatr Neonat Individual Med. 2015;4(2):e040207. doi: 10.7363/040207.

POSTER PRESENTATIONS

ABS 1

TRANSITIONAL CHANGES IN CEREBRAL BLOOD VOLUME OF TERM AND PRETERM INFANTS WITH AND WITHOUT RESPIRATORY SUPPORT AFTER BIRTH

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INTRODUCTION

Near-infrared spectroscopy (NIRS) is a non-invasive method to measure changes in the concentration of oxygenated (ΔO_2Hb) and deoxygenated hemoglobin (ΔHHb). Changes in total hemoglobin ($\Delta cHb = \Delta O_2Hb + \Delta HHb$) give information on changes in cerebral blood volume (ΔCBV). Recently, our study group has shown a significant decrease of CBV during immediate postnatal transition in healthy newborns. Up to now, no study investigated the transitional behavior of CBV in term and preterm infants with and without respiratory support (RS).

PATIENTS AND METHODS

This single-centre observational study was conducted at the Division of Neonatology of the Medical University of Graz. Term and preterm infants with and without respiratory support after caesarean section were included. NIRS measurements were conducted using NIRO®-200NX (Hamamatsu; Japan) over the first 15 minutes after birth. NIRS derived ΔHbT values were converted to ΔCBV. The difference of each value to the value at the 15th minute after birth was calculated for every minute within the study period. Moreover the tissue oxygenation index (cTOI) was evaluated using NIRS. Additionally preductal arterial oxygen saturation (SpO_2) and heart rate (HR) were continuously monitored by a pulse oximeter. Two groups were compared based on need for RS: RS and normal transition (NT) group.

RESULTS

We included 45 preterm infants (37 with and 8 without RS) and 159 term infants (19 with and 140 without RS) at a mean gestational age of 33 ± 2 and 39 ± 1 weeks, respectively. RS (NT) group consisted of 56 (148) neonates. Altogether we included 204 infants. There were no differences in heart rate between RS and NT group, but we found significant differences in regard to SpO_2 and cTOI, both showing higher values in NT group.

ΔCBV: A significant decrease in CBV of 1.0 ± 1.9 ml/100 g brain (mean ± SD) was shown within the first 15 min after birth in our study population ($p < .001$). We observed higher ΔCBV values in NT group compared to RS group, representing a pronounced decrease of CBV in NT group during the study period. Differences of ΔCBV between groups reached statistically significance ($p < .05$) at minutes 2, 6 and 7 and borderline significance ($p < .10$) at minutes 3, 4 and 5.

CONCLUSIONS

We observed differences in the behaviour of cerebral blood volume during immediate postnatal transition by comparing two groups of preterm and term infants based on requirement of respiratory support. There was a pronounced decrease of cerebral blood volume in infants without respiratory support.

ABS 2

HEMATOLOGIC ABNORMALITIES IN THE FIRST 72 HOURS OF LIFE IN SMALL-FOR-GESTATIONAL-AGE PRETERM NEWBORNS

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INTRODUCTION

Hematologic abnormalities are often reported in small-for-gestational-age (SGA) newborns. Traditionally, polycythemia is considered to be the most common hematologic disorder in this population, which has it's origin in chronic intrauterine hypoxia. Some recent data show that in preterm SGA newborns anemia is more often

present than polycythemia, especially in those with gestation under 34 gestational weeks. Leucopenia and thrombocytopenia have also been found in SGA preterm infants in some studies.

PATIENTS AND METHODS

We retrospectively collected data from all single preterm newborns (gestational age of $24^{0/7}$-$36^{6/7}$ weeks) born between January 2011 and September 2012 in tertiary-care university hospital. Exclusion criteria for the study were: multiple birth, major congenital anomalies, karyotype or metabolic abnormalities, intrauterine infections (TORCH), deliveries with abruption of placenta, early-onset sepsis. The sample was subdivided into two groups, according to gestation: very-low-gestational-age (VLGA) group with < 32 gestational weeks, and low-gestational-age (LGA) group with ≥ 32 gestational weeks. All newborns with birth weight percentiles < 10 were considered as SGA. We extracted data about hematological values during first 72 hours of life.

RESULTS

A total of 524 preterm newborns met the inclusion criteria – 108 in VLGA and 416 in LGA group. In VLGA group there were 47 SGA and 61 AGA newborns, with mean gestations of 29.24 and 28.73 weeks, respectively. Polycythemia was found in one SGA newborn. Early anemia was found significantly more often in SGA group (46.81%; 22.59%). Leucopenia (31.91%; 3.28%), thrombocytopenia (40.42%; 4.92%) and severe thrombocytopenia (12.76%; 1.64%) were also significantly increased in SGA group.

In LGA group, there were 107 SGA and 309 AGA newborns, with mean gestations of 34.96 and 35.23, respectively. Polycythemia was found in one SGA and one AGA case. Frequency of early anemia was not significantly different between groups. Leucopenia (8.41%; 0.97%) and thrombocytopenia (12.15%; 0.97%) were sigificantly increased in SGA group. Severe thrombocytopenia was found just in SGA group.

CONCLUSIONS

In our study sample, in SGA preterm newborns hematologic values in all three cell lines were significantly more often disturbed comparing with AGA preterms of similar gestation. Polycythemia was rare, but early anemia was significantly more often present in SGA newborns with very low gestation. Leucopenia and thrombocytopenia, including severe form of thrombocytopenia, were more often found in SGA preterm newborns of any gestational age.

ABS 3

THE ANTICOAGULANT ACTION OF ACTIVATED PROTEIN C IN VERY PRETERM INFANTS

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INTRODUCTION

There are unique differences in the newborn haemostatic system compared to the adult, with development dependent on gestational and postnatal age. However the very preterm haemostatic system is poorly characterised. Activated Protein C (APC) is one of the primary physiological inhibitors of thrombin generation. We hypothesized that prospective characterization of thrombin generated in preterm neonatal samples in the presence of APC would characterise APC regulation in the premature haemostatic system.

PATIENTS AND METHODS

In a prospective observational study, blood was drawn into citrated tubes from cord blood of neonates < 30 wks and on day 1 from non-heparinised lines. Exclusion criteria included antenatal intraventricular haemorrhage or parental bleeding disorder. Preanalytical variables were controlled for by ensuring samples were correctly filled, not clotted, and majority drawn by lead investigator. Platelet poor plasma was obtained by centrifugation of whole blood at 3,000 rpm for 10 min. Tissue factor (TF)-stimulated thrombin generation was characterized in a calibrated automated thrombography assay with 1 pM TF stimulus using Thrombinoscope™ software and repeated in presence of 2.5 nM APC and 1 nM APC. Control plasma was obtained from cord blood of term neonates.

RESULTS

Between April 2013 and April 2015, 137 patients < 30/40 were admitted, 11 were excluded and 126 recruited. Median (25^{th}-75^{th}) gestational age and birth weight was 27.7 (26.3-28.7) wks and 1,020 (818-1,221) g respectively. Analysis of procoagulant and anticoagulant mechanisms was performed in subset of infants where sufficient plasma was available. Endogenous thrombin potential and peak thrombin generated were comparable in preterm and term infants (p = 0.08, p = 0.4) (**Fig. 1**). Thrombin generation was dose dependently suppressed in the

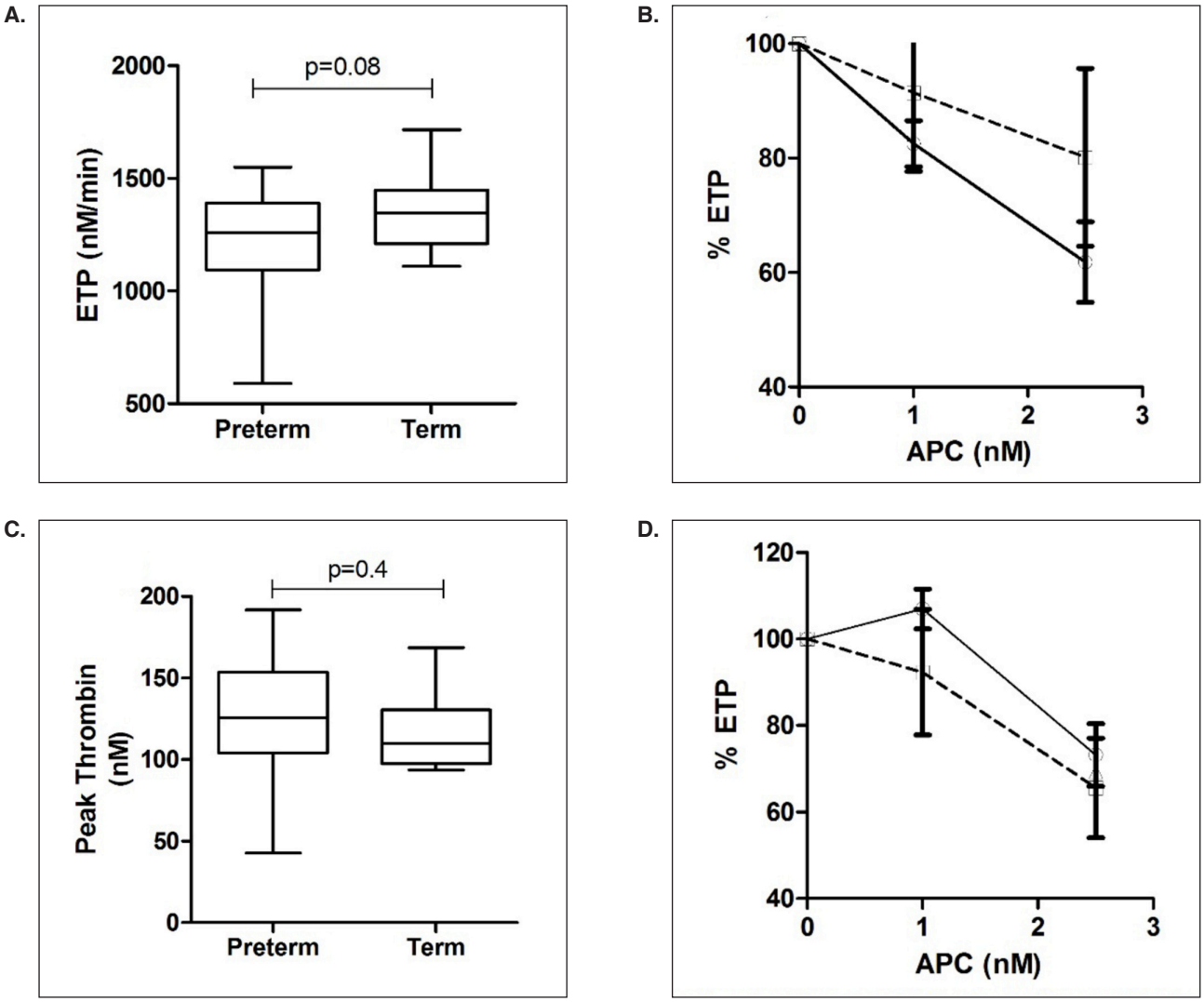

Figure 1 (ABS 3). Tissue factor (TF)-stimulated, phospholipid-dependent thrombin generation (n = 15 preterm infants; n = 13 term infants; C-G) in platelet poor plasma prepared from cord blood. **A, C.** Endogenous thrombin potential (ETP) and peak thrombin was measured. **B, D.** The effect of increasing doses of activated protein C in preterm infants (dashed line) and term infants (solid line) was measured.

presence of increasing amounts of APC in both cord samples from term and preterm neonates and in preterm neonatal samples. Suppression of thrombin generation by APC in preterm and term infants was non-significantly different (p = 0.03 ANOVA).

CONCLUSIONS

In the largest prospective study to date of very preterm infants, we describe the anticoagulant effect of activated protein C in preterm infants.

ABS 4

SURVIVAL AFTER CARDIAC ARREST IN THE NEONATAL INTENSIVE CARE UNIT

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INTRODUCTION

Mortality during cardiopulmonary resuscitation (CPR) for newborns in the delivery room setting is associated with both lower birth weight and CPR duration for more than 10 minutes. Characteristics and outcomes of CPR performed in the neonatal intensive care unit (NICU) setting may be distinct from the delivery room, due to differences in underlying pathophysiology. Both the incidence of cardiac arrest in the NICU and survival characteristics after CPR in the NICU are poorly described. Our study objectives were to identify the incidence of cardiac arrest requiring CPR in

a referral NICU and to determine the association between CPR duration and survival to hospital discharge.

PATIENTS AND METHODS

This was a retrospective cohort study of infants admitted from January 1, 2011-April 15, 2015 at the Children's Hospital of Philadelphia referral NICU. We used the hospital-wide resuscitation database to identify all infants with an acute cardiopulmonary arrest who required CPR (chest compressions for heart rate = 1 CPR event) and the data from the first event was used for the outcome of survival to discharge. The secondary outcome was survival during resuscitation, using all CPR events. We determined the association between duration of chest compressions and survival to discharge using Wilcoxon rank sum test.

RESULTS

There were 163 CPR events occurring in 109 infants during the study period. There were 1.2 CPR events per 1,000 patient-days in the NICU. The duration of chest compressions ranged from 1 minute to 53 minutes, with a median duration of 2 minutes (intra-quartile range [IQR] 1-4 minutes).

Of 109 infants who had at least 1 CPR event, 38 (35%) died before hospital discharge. Median duration of chest compressions was significantly shorter in infants who survived to hospital discharge (1 minute, [IQR 1-2] vs. 3 minutes, [IQR 1-16]), $p < 0.001$. Death occurred during CPR in 12/163 (7%) CPR events. Median duration of chest compressions was significantly shorter during CPR events that resulted in survival (2 [IQR 1, 3] vs. 18 [IQR 7, 25]), $p < 0.001$. The relationship between survival outcomes and duration of chest compressions are shown in **Fig. 1**.

CONCLUSIONS

CPR events are relatively rare in NICU patients. Shorter duration of chest compressions is significantly associated with survival to hospital discharge. Fewer than 10% of infants with CPR lasting > 5 minutes survived to hospital discharge. Future studies should focus on patient and performance characteristics that are associated with survival after CPR in the NICU.

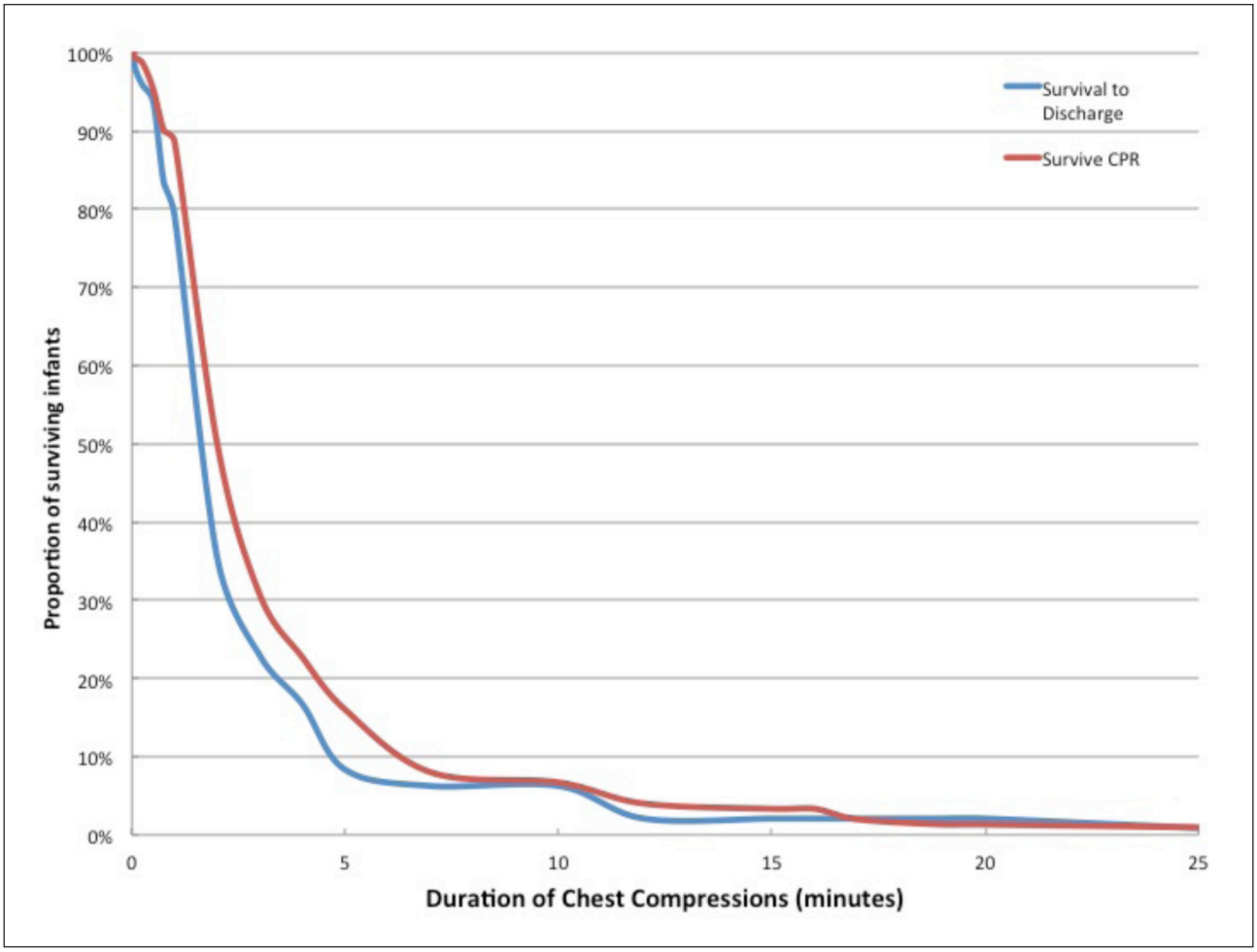

Figure 1 (ABS 4). Relationship between survival outcomes and duration of chest compressions.

ABS 5

A PATENT DUCTUS ARTERIOSUS SEVERITY SCORE INCORPORATING MARKERS OF HAEMODYNAMIC SIGNIFICANCE AND LEFT VENTRICLE DIASTOLIC FUNCTION PREDICTS CHRONIC LUNG DISEASE

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INTRODUCTION

The aetiology of chronic lung disease (CLD) in preterm infants is multi-factorial. Although an association between a patent ductus arteriosus (PDA) and CLD does exist, the cause and effect relationship is not established. The presence of early left ventricle (LV) diastolic dysfunction in the setting of increased pulmonary blood flow associated with a PDA may be a contributory factor in the evolution of CLD. We hypothesized that a PDA severity score incorporating markers of pulmonary overcirculation and LV diastolic function can predict the evolution of CLD (defined as the need for oxygen by 36 corrected weeks) or death before discharge in preterm infants.

PATIENTS AND METHODS

This was a multi-centre prospective observational study of infants < 29 weeks gestation. No PDA treatment was carried out in the first 5 days. An echo was carried out at a median of 43 hours of life (IQR 38-47) to measure PDA diameter and maximum flow velocity (V_{max}), markers of pulmonary overcirculation (left ventricular output [LVO]; Left atrial to aortic root ratio; mitral valve E wave to A wave ratio), markers of systemic hypoperfusion (diastolic flow in the descending aorta and celiac trunk), and parameters of LV function using tissue-Doppler imaging (s', e', a'). Predictors of CLD/death were identified using logistic regression models. A PDA severity score (PDAsc) was created and a receiver operating characteristic curve was constructed to assess its ability to predict CLD/death.

RESULTS

We included 141 infants with a mean (SD) gestation and birthweight of 26 (1.4) weeks and 952 (235) grams with 79 (56%) developing CLD/death. Multivariable logistic regression demonstrated that 5 parameters were independently associated with CLD/death: gestation (OR 0.3, $p < 0.001$), PDA diameter (OR 2.2, $p = 0.07$), V_{max} (OR 0.3, $p = 0.02$), LVO (OR 1.008 per 1 ml, $p = 0.03$) and LV a' wave (OR 0.6, $p = 0.01$). A PDAsc was constructed from the beta coefficients to yield a score from 0 (low risk) to 14 (high risk). Infants who developed CLD/death had a higher score than those who did not (**Fig. 1A**). PDAsc had an AUC of 0.92 (95% CI 0.86-0.97, $p < 0.001$) for the ability to predict CLD/death. A cut off of 5 has sensitivity, specificity, positive and negative predictive values of 92%, 87%, 92% and 82%. There was a strong relationship between the predicted probability for CLD/death and PDAsc (**Fig. 1B**).

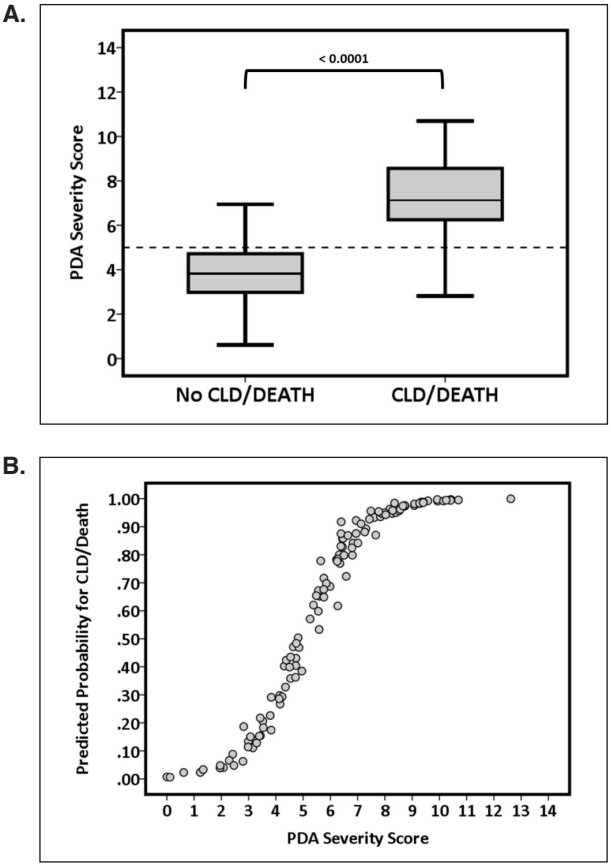

Figure 1 (ABS 5). A. Relationship between PDA severity score (PDAsc) and outcomes (CLD/death). **B.** Relationship between predicted probability for CLD/death and PDAsc.

CONCLUSIONS

Low LV diastolic function in the setting of increased pulmonary circulation associated with a PDA may contribute to the evolution of CLD. This PDA severity score may pave the way for a more targeted approach to PDA treatment.

Microcirculation and oxygen transport

ABS 6

A STUDY TO VALIDATE THE DURATION OF ASSESSMENT OF BASELINE NIRS VALUES IN PRETERM BABIES WITH ECHO-CARDIOGRAPHICALLY-CONFIRMED PDA

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INTRODUCTION

Near-infrared spectroscopy (NIRS) measures tissue oxygen saturation and is increasingly used in neonatal research to assess cerebral haemodynamics. The optimal range of NIRS variables is under debate and studies demonstrate significant variation on study methodology with varying length of measurement. In order to contribute to standardized methodology, this preliminary study aimed to explore the duration of observation needed to establish a baseline value for cerebral Tissue Oxygenation Index (TOI). We hypothesised that the duration of monitoring has no impact on the absolute TOI value.

PATIENTS AND METHODS

Measurements were obtained using the NIRO®-200NX oximeter (Hamamatsu Photonics, Japan) in the first day after recruitment during the first 3 days of life. The optodes were placed on the frontoparietal region and secured in place with a cohesive bandage. The median, standard deviation and coefficient of variance of TOI value was calculated for 1, 3, 5, 10, 20, 30, 60, 90 and 120 min epochs: each epoch was summarized once for each baby starting 10 minutes after the optodes were sited. The 120 min epoch was taken as the "gold standard" and the difference between the mean (SD) for the 120 min epoch was compared to the mean (SD) for each of the other epochs. Inclusion criteria included: neonates 24 to 28^{+6} weeks' gestation, postnatal age ≤ 72 hours, PDA confirmed echocardiographically.

RESULTS

We recruited 10 patients, mean age at recruitment 32 hours (range 6-65), mean birth weight 0.88 (SD 0.28), mean gestational age 26.4 (SD 1.45). The TOI value over 120 minutes and the values over other durations are summarized in **Fig. 1** and **Tab. 1**. One participant had a TOI < 55 during

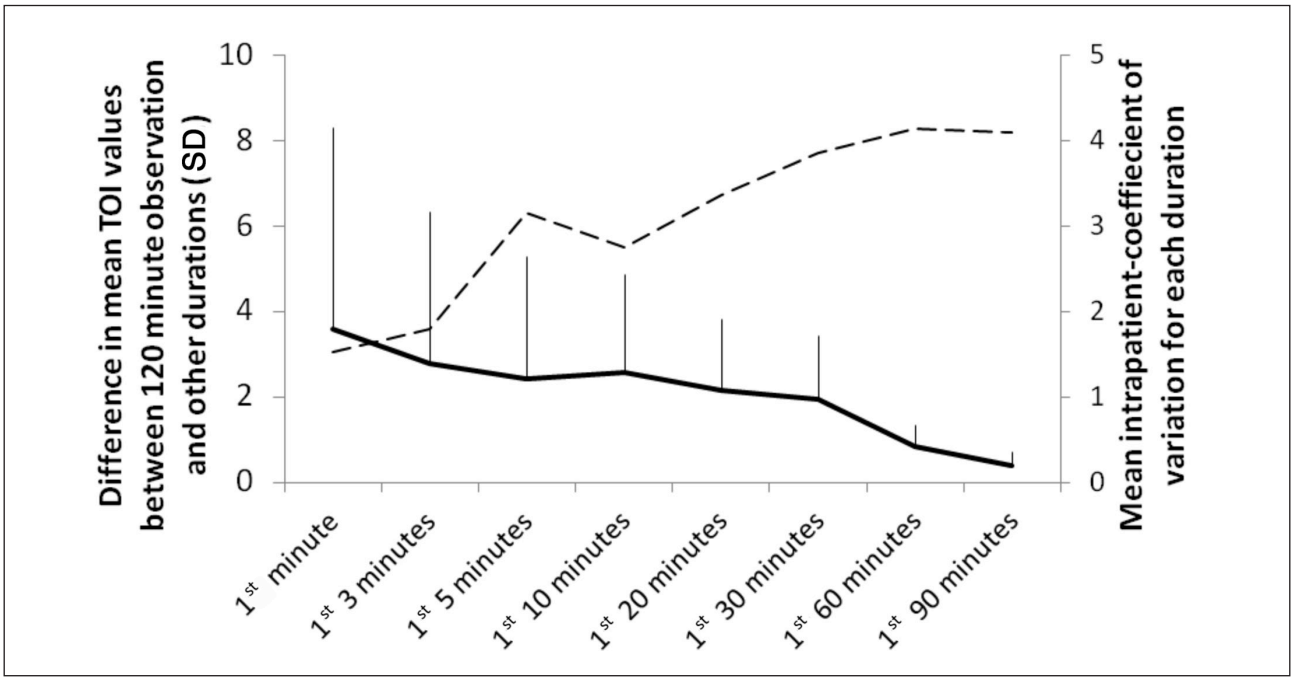

Figure 1 (ABS 6). Difference in mean Tissue Oxygenation Index (TOI) values between 120 minute observation and other durations. Mean intrapatient-coefficient of variation for each duration.

Table 1 (ABS 6). Tissue Oxygenation Index (TOI) values over 120 minutes.

	1st minute	1st 3 minutes	1st 5 minutes	1st 10 minutes	1st 20 minutes	1st 30 minutes	1st 60 minutes	1st 90 minutes	1st 120 minutes
Mean	70.7	70.7	70.0	69.4	69.3	69.9	70.1	70.2	70.4
SD	13.2	13.2	11.3	10.5	10.9	10.9	10.4	10.0	9.7
Min	52.5	51.8	52.4	52.1	50.2	49.9	49.9	50.7	51.8
Max	99.0	99.0	91.1	87.0	87.7	88.2	85.9	85.0	84.9

all durations. One participant had a TOI > 85 during the first hour but this was not sustained over two hours. The shorter durations showed greater differences from a two hour observation although the magnitude of the differences was relatively small. The mean intra-patient CV for each epoch increased as the durations increased suggesting that the shorter durations were less variable than the longer durations (**Fig. 1**).

CONCLUSIONS

The duration of observation affects the magnitude of the cerebral TOI. However, the differences between observation periods are small and are unlikely to be clinically or physiologically important. Summarising TOI over more than an hour may hide clinically significant changes.

These preliminary data suggest that regular documentation of TOI values during ongoing recordings can be based on short observation periods such as 1-3 minutes.

ABS 7

HAEMODYNAMICS IN PRETERM INFANTS WITH PATENT DUCTUS ARTERIOSUS (HAPI-PDA STUDY): A PILOT STUDY

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INTRODUCTION

Delayed closure of ductus arteriosus in premature neonates is associated with significant morbidity. Rather than considering patent ductus arteriosus (PDA) as being either present or not, it may be more appropriate to consider it as a disease spectrum ranging from biological normality to a pathological state associated with clinical instability with varying effects on organs. This study aimed to investigate this hypothesis by studying PDA characteristics simultaneously with biomarkers of brain activity and cerebral circulation.

PATIENTS AND METHODS

We conducted a pilot study to relate the size and haemodynamic effect of the PDA (as measured by echocardiographic biomarkers including PDA severity score, PDA size, PDA velocity, diastolic flow in the main pulmonary and left pulmonary artery [LPAf], biomarkers of diastolic function and fluid overload) with cerebral blood flow (measured by superior vena cava [SVC] flow), cerebral oxygenation (measured by tissue oxygenation index [TOI]) and cerebral electrical activity (measured by amplitude integrated electroencephalogram [aEEG]). Inclusion criteria were: neonates 24 to 28^{+6} weeks' gestation, postnatal age ≤ 72 hours, PDA confirmed echocardiographically and parental informed consent. Only data from the first day after recruitment were analysed.

RESULTS

We recruited 14 patients in 5 months. Median age at recruitment 38 hours (range 8-61), mean birth weight 0.92 kg (SD 0.25) and mean gestational age 26.6 weeks (SD 1.2). Mean PDA score 11.2 (SD 4.3) (**Tab. 1**), TOI 69.6 (SD 9), median aEEG

Table 1 (ABS 7). Echocardiographic parameters (first scan after birth).

Ductal features		
Transductal diameter (mm)	0.95[a]	0.36[b]
Ductal velocity V_{max} (m/s)	1.92	0.68
Magnitude of ductal shunt		
PDA:LPA diameter	0.31[a]	0.29[b]
Antegrade PA diastolic flow (cm/s)	23.5	14.6
Antegrade LPA diastolic flow (cm/s)	27.7	17.9
Left atrial:aortic ratio	1.33	0.38
Left ventricular:aortic ratio	1.77	0.31
Features of myocardial performance		
LVO/SVC flow ratio	1.35	0.76
E wave/A wave ratio	0.73	0.18
IVRT (ms)	44.6	7.4
PDA score	**11.2**	**4.3**

Data expressed as mean (SD) for continuous parametric outcomes. [a]Median and [b]interquartile ranges (IQR) for non parametric outcomes.

score 4 (range 0-10), SVC flow 116.8 ml/kg/min (SD 32.4). Data acquisition was feasible for 95% of time points. No adverse events were reported. Infants tolerated the study well. There was no significant association between PDA severity score and aEEG score or TOI or between the variability of aEEG score or TOI (**Fig. 1** and **Tab. 2**). PDA size was significantly correlated with LPAf and left ventricular: aortic root ratio ($p < 0.05$). There was a trend for statistical significant correlation between TOI and birth weight (r^2: 0.174, $p = 0.06$); PDA size and aEEG score (r^2: 0.2, $p = 0.08$). This pilot study has also identified areas for improvement in methodology that have already applied.

Table 2 (ABS 7). Mean scores of different parameters.

	Range	Mean	SD
TOI	0-100%	69.64	9
aEEG score	0-13	3.9	2.9
PDA score	0-27	11.2	4.3
SVC flow	Normal > 51 ml/kg/min	116.8	32.4

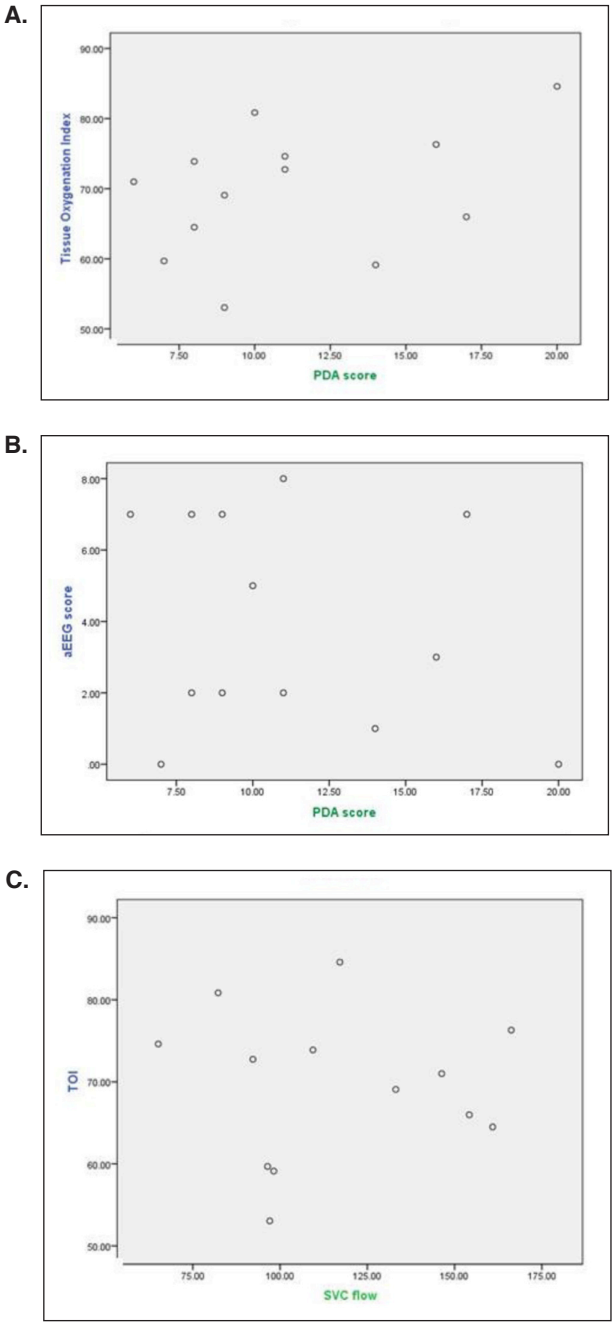

Figure 1 (ABS 7). A. Relation of cerebral oxygenation to patent ductus arteriosus (PDA) severity score. **B.** Relation of cerebral electrical activity to PDA severity score. **C.** Relation between tissue oxygenation index (TOI) and superior vena cava (SVC) flow.

CONCLUSIONS

This pilot study has not so far demonstrated any significant association between PDA severity and cerebral activity or cerebral oxygenation. Patients now being recruited have no demonstrable PDA and these will form a comparison group.

ABS 8

SKIN MICROCIRCULATION IN ASPHYXIATED NEWBORNS TREATED WITH HYPOTHERMIA

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INTRODUCTION

Therapeutic hypothermia (TH) decreases the metabolic demand and has become standard treatment for severe and moderate hypoxic-ischemic neonatal encephalopathy (HIE). In HIE infants oxygen delivery may fail to sustain cellular metabolism and organ function. By noninvasively assessments of skin microcirculation with use of Laser Doppler Perfusion Measurements (LDPM), Computer Assisted Video-Microscopy (CAVM) and Diffuse Reflectance Spectroscopy (DRS) during TH and after rewarming, we wanted to describe the changes in microvascular morphology and function induced by TH in HIE infants.

PATIENTS AND METHODS

A prospective study of 28 HIE infants who fulfilled the Norwegian National Guidelines for TH was conducted (median [range] GA 39.7 [36.0-41.9]

week, BW 3,486 [2,117-5,200] g, 10 min Apgar score 5.0 [0-9], umbilical artery pH 6.92 [6.59-7.19], lactate 15.5 [5.0-29.0], base deficit 13.7 [4.5-24.0]). They underwent whole-body TH for three days (33.5°C). Twenty-five healthy term neonates served as controls. LDPM was used for quantification of blood cell flux. A handheld digital assisted CAVM was used to obtain film sequences from the skin measuring capillary density and capillary flow velocity. Microvascular oxygen saturation was obtained by DRS. Chest skin examinations was performed day one and three of TH and day four after rewarming.

RESULTS

Survival rate was high (93%). Two died during hospital stay; one within 24 hours due to multiorgan failure, the other day 27 after redirection of care due to severe clinical and cerebral MRI pathology. Six had severe and 13 minor MRI pathology at day eleven, while seven had completely normal MRI findings.

LDPM significantly decreased during cooling ($p < 0.01$). LDPM after rewarming was equal to LDPM in controls. Functional capillary density was significantly higher during and after TH compared to controls ($p < 0.01$). Capillary flow velocity was significantly reduced during cooling ($p < 0.05$), normalized after rewarming. Tissue oxygen extraction was significantly higher during TH than after rewarming ($p < 0.01$), normalized after rewarming.

CONCLUSIONS

Infants with HIE had decreased perfusion, increased capillary density and oxygen extraction during TH. Reduced oxygen delivery is explained by reduced capillary flow velocities and increased velocity heterogeneity. The body's compensatory mechanisms to sustain the cellular respiration during cooling despite reduced perfusion and impaired oxygen diffusion are most likely the pathophysiological explanation for these findings. The asphyxiated insult per se may have contributed to the results.

ABS 9

PLETH VARIABILITY INDEX IN PRETERM INFANTS: IS IT FEASIBLE?

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INTRODUCTION

The Pleth Variability Index (PVI) is a parameter based on the changes in the Perfusion Index (PI) during a complete respiratory cycle. It represents the variation of the plethysmographic waveform due to respiration. PVI can be measured continuously by Masimo® pulse oximeters (Masimo Corp., Irvine, CA, USA). Related to changes in pulse pressure (PP) and sensitive to changes in ventricular preload, it is claimed that PVI predicts fluid responsiveness. Mainly studied in adults, the value of this parameter in preterm neonates is not well known. The aim of this study was to assess the reproducibility of the PVI in preterm neonates below 32 weeks of gestational age.

PATIENTS AND METHODS

To assess the PVI reproducibility between limbs and on the same limb, three measurements were consecutively performed in stable and comfortable preterm neonates in the first 48 hours of life. During each measurement, two pulse oximeter sensors simultaneously measured on two different limbs for five minutes. The first measurement compared left wrist vs. right wrist. The second measurement compared right foot vs. right wrist. The third measurement compared right foot vs. left foot. Reproducibility of the measurement was assessed with paired T test, the intra-class correlation coefficient (ICC) and Bland-Altman analysis.

RESULTS

A total of 25 preterm neonates were included. For each sensor side the average PVI during 300 seconds was calculated. Inter limb comparison showed fair to moderate intra class correlation coefficients (ICC) with 95% confidence intervals (95% CI): left hand-right hand ICC = 0.504 (0.114-0.759), right foot-right hand 0.470 (0.071-0.740) and right foot-left foot ICC = 0.310 ([-0.089]-0.623). Intra limb comparison showed fair to moderate for right foot-right foot ICC = 0.386 ([-0.021]-0.684) and good ICC for right hand-right hand 0.731 (0.455-0.879). Bland Altman plots showed moderate reproducibility of measurement between different limbs and of the same limb in consecutive time periods, with large biases and a wide 95% limits of agreement.

CONCLUSIONS

This study highlights that PVI measurement is poorly reproducible when measured on different limbs and on the same limbs in consecutive time periods in stable and comfortable preterm neonates. PVI therefore seems not feasible in the care of critically ill preterm neonates.

ABS 10

VALIDITY OF BIOMARKERS ON CARDIOVASCULAR SUPPORT (CVS): AN ANALYSIS IN RETROSPECT

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INTRODUCTION

Evidence supporting use of CVS for circulatory impairment early after birth in the premature infant is weak. Yet, no validated score system to define the condition is available. A single centre recently conducted a randomised placebo (PL)-controlled trial on dobutamine (DB) for low superior vena cava (SVC) flow in preterm infants with gestational age (GA) < 32 weeks (Bravo et al., submitted). We aimed to analyse in this cohort which biomarkers moved clinicians to initiate open label CVS in the normal SVC flow group and to assess the predictive capacity for adverse outcome (AO) of these biomarkers in the face of a future confirmatory trial (NeoCirc CTs-FP7; HEALTH-2011.4.2-1).

PATIENTS AND METHODS

Enrolled infants (low SVC flow group = 28; normal SVC flow group = 98) had intensive follow-up of blood pressure (MBP), lactate, base excess (BE) and SVC flow during the first 96 h. Infants were randomised to receive DB (n = 16) or PL (n = 12) if SVC flow < 41 ml/kg/min within 24 h from birth. Main neonatal outcomes at term equivalence date were recorded. Biomarkers' threshold used for analyses: MBP < GA -1 mmHg; lactate > 4 mmol/L; BE < -9 mmol/L; SVC flow < 51 ml/kg/min. Statistics: Mann-Whitney rank-sum test, Fisher's exact test, binary logistic regression analysis and ANCOVA test.

RESULTS

37% of the infants in the normal SVC flow group received CVS; 17% received at least 1 catecholamine (age range 2-24 h). MBP 4 mmol/L were the most prevalent biomarkers at start on treatment; 20% of infants had 2 or more biomarkers. SVC flow < 51 ml/kg/min (OR 2.5; 95% CI 1.0-5.9; p) and lactate > 4 mmol/L (OR 5.2; 95% CI 1.2-21.3; p < .024) present at 12 h from birth predicted combined AO (death or severe brain injury). SVC flow < 51 ml/kg/min (OR 4.3 95% CI 1.3-13.5; p) and lactate > 4 mmol/L (OR 5.5; 95% CI 1.3-23.0; p < .019) present at 12 h from birth predicted death. MBP < GA -1 mmHg or MBP < GA -5 mmHg did not.

CONCLUSIONS

Low SVC flow and lactate are the earliest predictors of AO. Both biomarkers should be included to monitor treatment effect in a placebo-controlled trial on CVS for early circulatory impairment in the preterm infant.

ABS 11

PILOT STUDY OF DOBUTAMINE (DB) VERSUS PLACEBO (PL) FOR EARLY LOW SUPERIOR VENA CAVA (SVC) FLOW: LONG-TERM OUTCOME

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INTRODUCTION

Low SVC flow during transitional circulation associates an increased risk for intraventricular haemorrhage, neurodevelopmental delay and death. Our group recently reported the efficacy of DB versus PL to treat this condition. There are no prospective long-term data on cardiovascular treatment compared to PL in preterm infants with circulatory impairment. We aim to assess the neurodevelopmental outcome at 2-3 years in infants with low SVC flow who were randomised to receive DB or PL.

PATIENTS AND METHODS

126 infants underwent early (< 12 h from birth) and serial (first 96 h) echocardiography and were randomised to DB (n = 16; step-wise dose increase: 5-10-15-20 μg/kg/min) o PL (n = 12; equal volume) if SVC flow < 41 ml/kg/min at any time during the first 24 h from birth. Structured clinical examination (quality of General Movements, GMs) and neurodevelopmental test (Bayley Scales II/III, BS) were scheduled between 2-3 years of age. Brain damage was classified according to the worst cranial ultrasound (cUS) before or at 36 weeks'gestation. Neurodevelopmental delay (NDD) was defined as BS score -2 SD or below.

RESULTS

Seventeen infants died (DB = 5, PL = 2, normal flow = 10). An abnormal cUS (intraventricular haemorrhage grade III or periventricular haemorrhagic infarction or persistent periventricular

echogenicity) was present in 36 (28%) infants (3 DB, 6 PL, 27 normal flow). 82% of survivors (DB = 8, PL = 9, normal flow = 72) were followed-up up to 2-3 years (complete 82 [75%]; 7 [6%] clinical exam only). Among these infants, 14 (16%) had NDD (1 DB, 1 PL, 12 normal flow); and 9 (10%) suffered cerebral palsy (CP) (0 DB, 1 PL, 8 normal flow). Combined adverse outcome (death or abnormal cUS or NDD or CP) was present in 45 infants (36%) in the full cohort (6 DB [37% within DB group], 7 PL [58% within PL group], 32 [33% within normal flow group]) ($p < 0.4$ between DB and PL groups).

CONCLUSIONS

This small pilot trial showed non-significant trends of higher survival free of neurodevelopmental impairment in the low SVC flow infant treated with DB compared to that receiving PL. These findings need to be confirmed in a randomised trial powered for a relevant clinical outcome.

Organ blood flow and autoregulation

ABS 12

THROMBOELASTOGRAPHYCAL ASSESSMENT OF THE HEMOSTATIC SYSTEM IN NEWBORNS WITH PERIVENTRICULAR HEMORRHAGE

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INTRODUCTION

The hemostatic system has differences among neonates, children and adults. Many coagulation variables constantly change in various diseases, such as hypoxia, infections and sepsis. Thromboelastography (TEG) is a whole blood coagulation test that provides a global assessment of hemostasis from clot initiation and development, to fibrinolysis (**Fig. 1**). TEG allows to determine the viscoelastic properties of clotting blood. The maximum amplitude of the TEG tracing is determined by the sum of the interaction of platelets and fibrinogen.

OBJECTIVES

To investigate the coagulation system of newborns with periventricular hemorrhage (PH) according TEG with platelet component of hemostasis.

PATIENTS AND METHODS

36 term infants, gestational age 37-41 weeks, were prospectively enrolled into the study. These patients did not have infections, congenital diseases, and their mothers were not receiving any anticoagulant therapy during pregnancy. The patients were divided into 2 groups: 8 infants with PH according neurosonography and 28 healthy newborns. As part of the routine screening platelet counts, mean platelet volume (MPV), platelet distribution width (PDW), platelet large cell ratio (P-LCR) were obtained from each child. Blood samples were collected by venous cannulation at

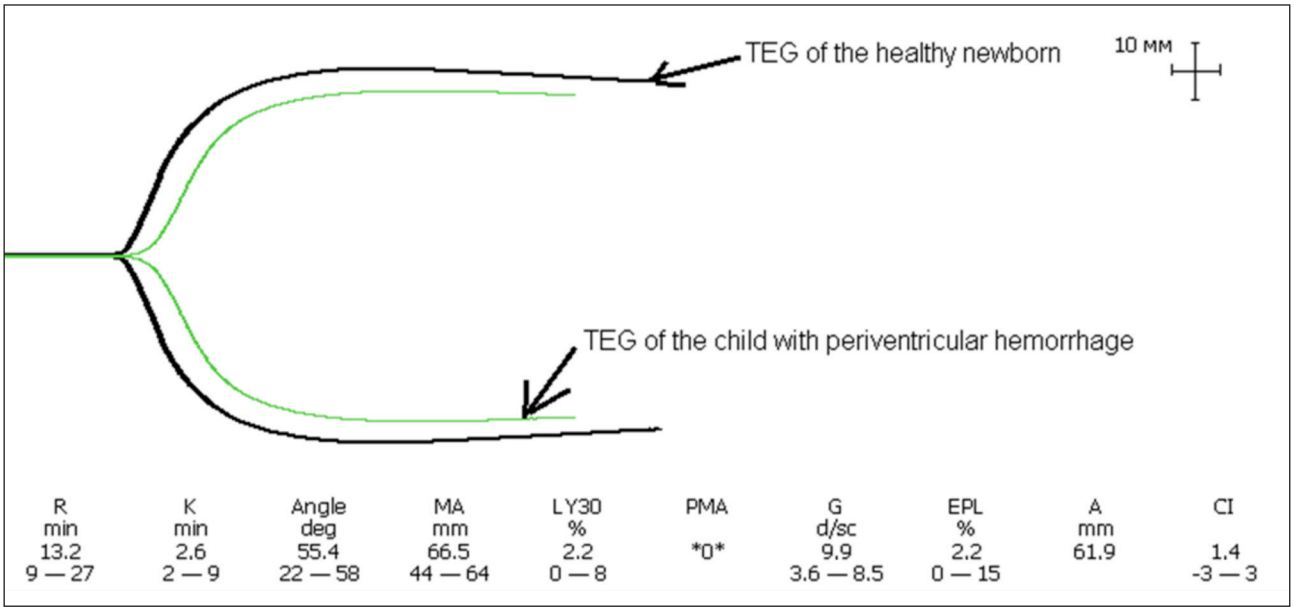

Figure 1 (ABS 12). Thromboelastography (TEG) of the healthy newborn and the child with periventricular hemorrhage.

2-3 days of life and conventional coagulation tests was performed. Clot reaction time (R), clot kinetics (K), maximum amplitude (MA), alpha angle and coagulation index (CI) were obtained from the TEG tracing (native citrated).

RESULTS

Platelet count did not differ significantly between two groups. MPV was statistically lower in group with PH (9.53 ± 0.77 fl) when compared to the healthy controls (10.22 ± 0.67 fl). PDW and P-LCR were 9.75 ± 0.82 and 20.67 ± 5.23% respectively in a group of children with PH and were lower compared to the control group (10.97 ± 0.67 and 26.08 ± 5.15% respectively). Prothrombin time, activated partial thromboplastin time and fibrinogen did not differ between groups. TEG-R values did not reach statistical significance between both groups. K was statistically higher in group with PH compared to the healthy infants (**Tab. 1**). The α angle, MA and CI were statistically lower in newborns with PH compared to the control group. Bivariate analysis showed a significant correlation between platelet count and MA of newborns with PH ($r = 0.821$; $p < 0.0500$), but no correlation in control group.

CONCLUSIONS

Hypocoagulation has been demonstrated in group with periventricular hemorrhage, that manifested prolongation of K, as well as a decrease α-angle, MA and low CI.

The disturbance of platelet hemostasis plays an important role in the genesis of periventricular hemorrhage, which is manifested by a decrease in MPV, PDW, P-LCR.

Newborns with periventricular hemorrhage should be performed TEG instead of routine coagulation tests, which are not informative.

Table 1 (ABS 12). Thromboelastography (TEG) variables of newborns with periventricular hemorrhage and healthy infant.

Variable	Newborns with periventricular hemorrhage	Healthy newborns	Z, p
Clot reaction time (R), min	14.5 ± 5.45	12.39 ± 4.66	Z = 1.18, p = 0.237
Clot kinetics (K), min	6.01 ± 2.54	3.91 ± 1.52	Z = 2.31, p = 0.021
Alpha angle (α), °	35.53 ± 9.57	46.97 ± 10.41	Z = -2.42, p = 0.016
Maximum amplitude (MA), mm	52.89 ± 9.05	59.73 ± 4.89	Z = -2.34, p = 0.019
Coagulation index (CI)	-0.56 ± 1.23	0.83 ± 1.20	Z = -2.27, p = 0.023

ABS 13

THE EFFECT OF ANTENATAL MAGNESIUM SULFATE ADMINISTRATION ON LEFT VENTRICULAR AFTERLOAD AND MYOCARDIAL PERFORMANCE MEASURED USING DEFORMATION AND ROTATIONAL MECHANICS IMAGING

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INTRODUCTION

Administration of antenatal magnesium sulfate ($MgSO_4$) can reduce cerebral palsy in preterm infants but its impact on early haemodynamics is poorly understood. We aimed to assess (1) the impact of $MgSO_4$ administration on left ventricular function measured using deformation and rotational mechanics imaging and (2) its impact on left ventricle (LV) afterload by measuring systemic vascular resistance (SVR) and LV wall stress.

PATIENTS AND METHODS

Preterm infants who were not in receipt of antenatal $MgSO_4$ were matched for gestation, birthweight and mode of delivery with infants that received $MgSO_4$. Echocardiography was carried out at a median of 11 hours of life (IQR 9 to 13) to measure global LV longitudinal strain (GLS), LV twist, untwist rate, right ventricle (RV) fractional area change (FAC), left ventricular output (LVO) and ejection fraction (EF). Heart rate and blood pressure were noted at the time of the scan. SVR and wall stress were calculated from the measured parameters.

RESULTS

Nineteen infants without $MgSO_4$ were matched with 19 infants who received $MgSO_4$. The median (IQR) gestation and birth weight of the cohort was 27.1 weeks (25.8-28.6) and 923 grams (810-1,073) respectively. There was no difference in the 5 minute Apgar score, cord pH, FiO_2, mean airway pressure or mode of ventilation between the groups (all $p > 0.5$). The $MgSO_4$ group had a significantly lower systolic blood pressure, SVR and a trend towards lower wall stress (**Tab. 1**). Infants in the $MgSO_4$ group had a significantly higher GLS, twist and untwist rate. Surrogates for systemic blood flow

Table 1 (ABS 13). Comparison of preterm infants without and with antenatal $MgSO_4$.

	No $MgSO_4$	$MgSO_4$	p
Gestation (weeks)	27.1 [25.8-27.7]	27.1 [26.0-28.0]	0.5
Birthweight (g)	925 [790-1,060]	880 [810-1,180]	0.7
Caesarean section	10 (53%)	10 (53%)	1.0
Complete course of antenatal steroids	7 (37%)	14 (74%)	0.06
Systolic BP (mmHg)	50 (11)	43 (5)	0.03
SVR (mmHg/kg/min)	291 [220-470]	238 [171-274]	0.03
Wall stress (g/cm^2)	23 (9)	18 (7)	0.06
LV GLS (%)	-12.7 (5.3)	-17.4 (3.6)	0.04
Twist (°)	4.1 (2.7)	8.8 (3.2)	0.01
Untwist rate (°/sec)	-54 (26)	-111 (59)	0.02
RV FAC (%)	29 [24-38]	40 [30-47]	< 0.01
LV ejection fraction (%)	55 (8)	60 (6)	0.03

Values are presented as median [IQR], means (SD) or count (%).

(EF and RV FAC) were also significantly higher in the $MgSO_4$ Group (**Tab. 1**). Those associations remained significant after adjusting for antenatal steroids.

CONCLUSIONS

$MgSO_4$ administration is associated with a lower afterload milieu in the immediate postnatal period. This translates to a higher myocardial function and systemic blood flow. This may partly explain the mechanism of its benefit in reducing cerebral palsy.

ABS 14

THE EFFECT OF MATERNAL ANTIHYPERTENSIVE DRUGS ON CEREBRAL, RENAL AND SPLANCHNIC OXYGEN EXTRACTION IN PRETERM BORN NEONATES

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INTRODUCTION

Mothers from preterm born infants often receive antihypertensive drugs due to preeclampsia or placental insufficiency (labetalol), for tocolysis (nifedipine), or as a neuroprotective agent (magnesium sulfate, $MgSO_4$). These drugs are known to cross the placenta, persist in the neonatal circulation for a few days after birth and possibly cause adverse hemodynamic effects in the fetus and neonate. We aimed to assess whether maternal antihypertensive drugs (MADs) affect neonatal regional tissue oxygen extraction, a measure for organ perfusion.

PATIENTS AND METHODS

Eighty preterm neonates ≤ 32 weeks of gestational age (GA) were prospectively included. Postnatal cerebral, renal and splanchnic oxygen saturations were monitored using near-infrared spectroscopy (NIRS). Mean cerebral, renal and splanchnic fractional tissue oxygen extractions (cFTOE, rFTOE, and sFTOE, respectively) were calculated for the first 5 days after birth. Newborns were categorized into exposure to labetalol ± $MgSO_4$, to nifedipine ± $MgSO_4$, to $MgSO_4$ only, and no exposure (controls). Using multilevel analysis corrected for statistically significant confounders, we determined the effect of various MADs on cFTOE and rFTOE. The relation between MADs and sFTOE was explored using the Kruskal-Wallis and Mann-Whitney U test.

RESULTS

Eleven infants were exposed to labetalol ± $MgSO_4$ (median gestational age [GA] 28.2 weeks, interquartile range [IQR] 26.7-28.6), 7 to nifedipine ± $MgSO_4$ [GA 28.1, IQR 25.0-29.3], 20 to $MgSO_4$ only [GA 28.1, IQR 27.7-29.5], and 42 to no MADs at all [GA of 28.1, IQR 26.7-29.3]). Compared to controls and corrected for head circumference, the cFTOE of newborns exposed to labetalol ± $MgSO_4$ was 41.08% (p = 0.02), 43.58% (p = 0.01), and 32.52% (p = 0.02) lower on day 1, 2, and 4, respectively. On day 2, cFTOE was also lower in newborns exposed to nifedipine ± $MgSO_4$ (43.03%, p = 0.02) and to $MgSO_4$ only (28.22%, p = 0.04). sFTOE, in contrast, was significantly higher in

infants exposed to labetalol ± $MgSO_4$ on day 1 (μ = 0.71) and 2 (μ = 0.82) than in non-exposed infants (μ = 0.23, p = 0.04 and μ = 0.55, p = 0.007, respectively). rFTOE was not influenced by MADs (p > 0.05), corrected for GA and $paCO_2$ of the first 48 hours.

CONCLUSIONS

We found a decreased cFTOE on days 1, 2 and 4, and an increased sFTOE on days 1 and 2. The decrease in cFTOE may be related to either increased cerebral perfusion or neurologic depression induced by the medication itself, or preferential brain perfusion associated with placental insufficiency (fetal brain-sparing). The latter is supported by the concomitant increase in sFTOE. rFTOE remained stable, which may be related to renal autoregulation.

ABS 15

SERUM NEUTROPHIL GELATINASE-ASSOCIATED LIPOCALIN AS AN EARLY MARKER OF ACUTE KIDNEY INJURY IN NEONATES WITH HYPOPLASTIC LEFT HEART SYNDROME

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INTRODUCTION

Acute kidney injury (AKI) is a primarily described complication after unbalanced systemic perfusion in neonates with congenital heart defects, including hypoplastic left heart syndrome (HLHS). Neutrophil gelatinase-associated lipocalin (NGAL) is postulated to be a potentially new and highly specific and sensitive marker of AKI.

The aim of the study was to compare umbilical as well as 24 hours after birth NGAL levels between neonates born with HLHS and healthy infants, and to analyze whether the determination of NGAL level could predict AKI in neonates with prenatally diagnosed HLHS.

PATIENTS AND METHODS

Prospective cohort study was conducted from January 2012 to May 2014 in a third degree reference neonatal care unit in Katowice, Poland. Fourty-seven neonates, with prenatally diagnosed HLHS, were enrolled as the study group and 30 healthy neonates served as controls. Perinatal characteristics and postnatal parameters were extracted from the hospital neonatal database. Blood samples were collected from umbilical cord blood and peripheral vein 24 hours after birth in all enrolled newborns. We assessed serum molality as well as serum NGAL, creatinine and lactate levels in all cases.

RESULTS

Elevated NGAL levels were observed among 9 neonates with HLHS and diagnosed AKI stage 1, in comparison to those newborns without AKI, both in umbilical cord blood (94.7 [58.6-130.9] ng/ml vs. 36.5 [26.9-46.0] ng/ml; p < 0.001) and 24 hours after birth (137.5 [81.9-193.1] ng/ml vs. 40.9 [32.5-49.2] ng/ml; p < 0.001). However, we observed a significant increase in the concentration of creatinine after 24 hours in neonates with AKI in comparison to healthy children (1.5 [1.2-1.7] mg/dl vs. 0.9 [0.8-0.9] mg/dl; p < 0.001). Furthermore, it was noticed that in newborns with HLHS and AKI, there was a significantly lower serum molality 24 hours after birth in comparison to umbilical cord blood molality (279.1 [275.0-283.2] mmol/kg H_2O vs. 284.0 [280.2-287.8] mmol/kg H_2O). Initial serum NGAL in umbilical cord blood and 24 hours after birth could predict, with high sensitivity and specificity, AKI in neonates with HLHS.

CONCLUSIONS

Elevated serum NGAL measured in umbilical cord blood and 24 hours after birth reliably indicate AKI in neonates with HLHS.

ABS 16

A PROSPECTIVE STUDY INTO THE GENERATION OF INDIVIDUALISED OPTIMAL MEAN ARTERIAL BLOOD PRESSURE (MABP) MEASUREMENTS USING NEAR-INFRARED SPECTROSCOPY (NIRS) IN THE PRETERM NEONATE

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INTRODUCTION

In the preterm neonate, disturbances in cerebral blood flow (CBF) are implicated in haemorrhagic and ischaemic pathology. Maintenance of a 'normal' mean arterial blood pressure (MABP) that ensures adequate perfusion of the brain is vital in the first hours of life. Previously, investigations into optimising adult cerebral perfusion pressure (CPP) have shown an

association between deviation from an individualised CPP level and bad outcome. Using a near-infrared spectroscopy (NIRS) sensor which measures a surrogate for CBF, the tissue oxygenation index (TOI), an optimal MABP (OptBP), where cerebral-vascular reactivity is strongest, can be computed. For OptBP to be clinically applicable, estimates need to be generated soon after monitoring is commenced.

PATIENTS AND METHODS

With informed parental consent, 33 preterm infants with a median (range) age of 26^{+6} (23^{+3}-31^{+0}) weeks gestation, and a median (range) weight of 793 g (540-1,350) were studied for the first 48 hrs of life. Using a NIRO®-200NX (Hamamatsu, KK, Japan), TOI was recorded continuously with MABP and stored using ICM+ (Cambridge, UK) software. Using Pearson's r between TOI and MABP over a 5-min window using 10-s averages an autoregulation index was constructed. Using a 4-hr sliding window, a histogram of MABP vs. TOI was constructed using a number of different parameters (**Tab. 1**) to generate 6 variations of the automatic U-shaped curve method where the curve's turning point was defined as OptBP (Aries et al., 2012). Percentage presence of OptBP over the whole study and in the first 6 hrs was analysed.

RESULTS

Optimal BP values were successfully calculated in 97% of subjects. In those where OptBP was calculated, mean percentage success (mean, SD; range) of detecting OptBP values was 31.0% (15.9; 2.1-63.8). When all methods were aggregated together using the median, percentage success increased to 51.2% (18.3; 18.6-86.3). No significance differences were found between any techniques (Kruskal-Wallis; p = 0.99) but significance was found when the aggregate OptBP was added (p < 0.001). In the first six hours of each study, OptBP was successfully calculated in 94% of subjects. The average OptBP percentage was 34.8 (27.9; 0.0-99.3) and when aggregated together OptBP value was 56.0 (31.8; 0.0-100.0). No significant differences were found between optimal MABP techniques (p = 0.99) and when adding the aggregate method (p = 0.064). Normality was determined by K-S test (p > 0.05), histogram and Q-Q plots.

CONCLUSIONS

Using a new aggregated technique of multiple histogram generating methods we have shown that the amount of continuous OptBP measurements made per patient can be increased by an average of 20% (**Fig. 1**). This method is successful in most

Table 1 (ABS 16). Parameters used to construct a histogram of mean arterial blood pressure (MABP) vs. tissue oxygenation index (TOI).

Method	Histogram Parameters			
	Min Value (mmHg)	Max Value (mmHg)	Number of Bins (k)	Bin Width (h)
1	12.0	80.0	24	2.0
1	12.0	80.0	$\left\lceil \frac{\max x - \min x}{h} \right\rceil$	2.0
2	Min of Data	Max of Data	$\sqrt{n}$	2.0
3	Min of Data	Max of Data	$\lceil \log_2 n + 1 \rceil$	2.0
4	Min of Data	Max of Data	$\left\lceil \frac{\max x - \min x}{h} \right\rceil$	$\frac{3.5\sigma}{n^{1/3}}$
5	Min of Data	Max of Data	$\left\lceil \frac{\max x - \min x}{h} \right\rceil$	$2\frac{IQR(x)}{n^{1/3}}$

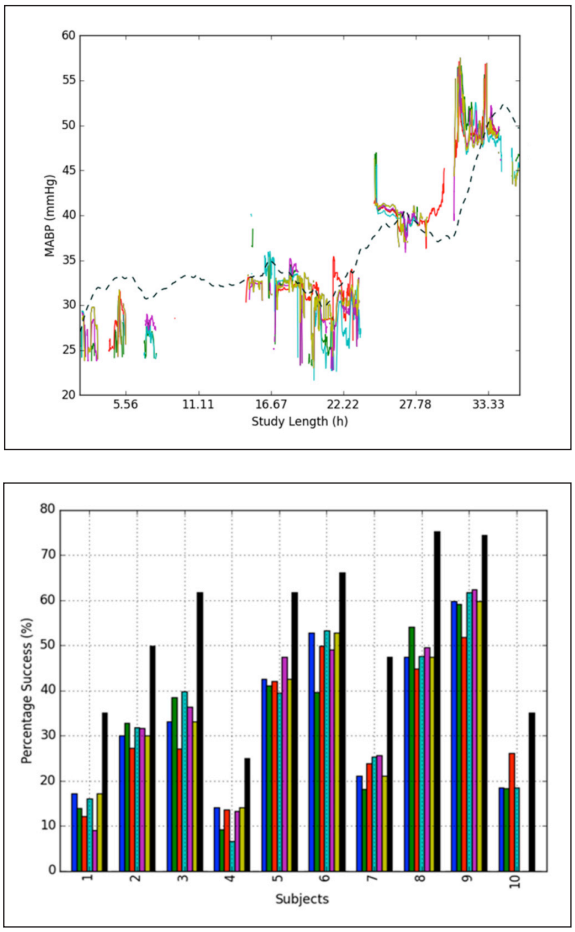

Figure 1 (ABS 16). Plot of Optimal BP (OptBP) plotted for different histogram variations (**A**) and the 4-hr rolling mean MABP (blue dotted line) of a single subject (**B**). Percentage success of OptBP measures across 10 subjects, black OptBP indicates the median grouping of all other OptBP measures (**B**).

patients and also is effective earlier in recording, which will add to the ability of continuous monitoring and calculation of OptBP to be performed earlier than previously reported.

Placenta and prenatal factors

ABS 17

THE EFFECTS OF SKIN-TO-SKIN ON PLACENTAL TRANSFUSION: A NONRANDOMIZED PILOT CONTROLLED TRIAL

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INTRODUCTION

The benefits of skin-to-skin and delayed cord clamping are two term birth practices endorsed by the World Health Organization. Skin-to-skin encourages bonding, improves thermoregulation and supports early initiation and duration of breastfeeding. Delayed cord clamping increases red cell volume and can boost infant iron stores during the first six months of life. Little is reported in the literature as to how these two practices interact. Placental transfusion is enhanced by gravity, time and contractions. When skin-to-skin, the infant is placed on the maternal abdomen above the level of the placenta. This may interfere with an infant receiving its full placental transfusion.

PATIENTS AND METHODS

A pilot controlled trial of 32 healthy term pregnant women and infants who were consecutively assigned to one of four umbilical cord clamping groups: immediate (< 10 seconds), delay of two minutes, delay of five minutes or cord milking (x 5). Infants were held skin-to-skin immediately after birth and remained for at least 30 minutes. Before delivery of the placenta, placental residual blood volume (PRBV) (the amount of blood left behind in the placenta and a proxy for the blood volume the infant did not receive) was drained into a blood collection bag and weighed. At 36-48 hours, infant capillary hematocrit and total serum bilirubin levels were measured. Infant well-being was assessed at 2, 7 and 14 days. The study was approved by the institutional review board.

RESULTS

No differences were reported in maternal and infant demographic and safety characteristics. Cord clamping time differed per assignment. Infants who received a five minute delay had a significantly lower PRBV (reported in ml/kg of birth weight) compared to infants who received immediate clamping ($p < 0.0001$) or a two-minute delay ($p < 0.005$). There was no significant difference in PRBV between the immediate and two-minute delay groups ($p = 0.14$). Total serum bilirubin levels did not differ across the four groups. Infants with a five-minute delay had a higher 36-48 hour hematocrit level compared to those receiving immediate clamping ($49.7 + 6.2$ vs. $60 + 3$, $p = 0.013$). None of the infants had a hematocrit level > 65%. Two infants in the immediate group had a hematocrit level < 47%. None of the infants received phototherapy while in-hospital.

CONCLUSIONS

When the infant is placed skin-to-skin after birth, waiting to clamp the umbilical cord for five minutes can promote a significantly higher placental transfusion compared to a two-minute delay or immediate clamping. A five-minute delay is a simple intervention that allows the infant held skin-to-skin to receive a full placental transfusion with no apparent adverse outcomes.

ABS 18

ASSOCIATION BETWEEN INDUCED LABOR AND FETAL STRESS HORMONE RELEASE

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INTRODUCTION

Vaginal delivery evokes a dramatic surge in fetal stress hormones, including arginine vasopressin (AVP), which supports infant's transition from intra-uterine to extra-uterine life. Oxytocin is widely used for the induction of labor at term and a prophylactic approach to 'prime' the fetus before planned caesarean section (PCS) in order to reduce neonatal morbidity has been proposed. However,

the relationship between induced labor before PCS and fetal stress response has not been investigated yet.

OBJECTIVE

To investigate the effect of induced labor prior to PCS on fetal copeptin release, a robust marker of AVP (primary endpoint), and on maternal and neonatal outcome (secondary endpoints).

PATIENTS AND METHODS

In a randomized, placebo-controlled trial 133 pregnant women with PCS were assigned to an oxytocin challenge test group (n = 66) or placebo group (n = 67). An infusion with 5 IU oxytocin in 500 ml Ringer's lactate solution was used for oxytocin challenge test with a minimum infusion rate of 12 ml/h. Infusion was stopped when three uterine contractions per 10 min were recorded. Inclusion criteria comprised, singleton pregnancies, gestational age more than 36 weeks, no contractions reported within the last 24 hours and on cardiotocography 30 minutes prior to trial start. Copeptin concentrations were measured in arterial umbilical cord blood at birth by a C-terminal pro-AVP luminescence immunoassay. Trial registration: clinicaltrials.gov identifier NCT01962701.

RESULTS

The administration of oxytocin (mean perfusion rate 26 ml/h) was well tolerated and did not result in non-reassuring fetal heart rate pattern or uncontrolled labor. Only 45% of women in the oxytocin group realized induced contractions. Gestational age, birth weight, arterial umbilical cord pH, and 5 min Apgar did not differ between groups. Arterial umbilical cord copeptin concentrations (median [range]) were three-fold higher in the oxytocin group than in controls: 22.2 pmol/L (3.2-2,319) vs. 7.39 pmol/L (2.5-344.6), $p < .001$. Postnatal infant weight loss was comparable in both groups (7.2 % ± 2.0 vs. 7.2% ± 2.3 [mean ± sd]). Four infants (6%) in the control group were admitted to neonatal care with respiratory distress syndrome compared to two (3%) in the oxytocin group ($p = 0.414$). 61% of infants in the oxytocin group needed breast-milk substitute vs. 73% in the control group ($p = 0.125$).

CONCLUSIONS

Uterine contractions induced by an oxytocin challenge test prior to PCS are sufficient to trigger sustained fetal copeptin release, indicating mild fetal stress response without causing any safety issues. Our data provide the framework for a large controlled trial to test whether induced mild fetal stress response prior to PCS may reduce neonatal morbidity such as respiratory distress syndrome.

Pulmonary Hypertension

ABS 19

ASSESSMENT OF PULMONARY HEMODYNAMIC FUNCTION IN PRETERM INFANTS: MATURATIONAL PATTERNS OF PULMONARY ARTERY ACCELERATION TIME

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INTRODUCTION

Pulmonary artery acceleration time (PAAT) derived by Doppler echocardiography is a non-invasive quantitative method used to study the blood flow velocity characteristics in the right ventricle outflow tract in response to changes in pulmonary vascular compliance and load. Characteristically, lower values of PAAT reflect elevated pulmonary vascular resistance and pulmonary artery pressures. The objectives of this study were to determine the maturational (age- and weight-related) changes of PAAT and to establish reference values in healthy preterm neonates.

PATIENTS AND METHODS

In this prospective observational study, PAAT was measured serially at 1, 2, 5-7 days of age, and 36 weeks post menstrual age (PMA). Standard views across the pulmonary valve were used to measure the time interval from the onset of systolic pulmonary arterial flow to the peak flow velocity. The PAAT was adjusted for right ventricle ejection time (RVET) using the ratio of the PAAT:RVET. A sub analysis of infants with chronic lung disease, defined as need for any respiratory support at 36 weeks PMA, was

performed. Two blinded observers assessed inter- and intra-observer reproducibility using Bland Altman analysis (bias, 95% limits of agreement [LOA]), coefficient of variation (CV), and correlation using linear regression.

RESULTS

218 preterm infants with a mean (SD) gestation and birth weight of 26.8 (1.4) weeks and 949 (224) g, respectively were included. There was an increase in PAAT from birth to 36 weeks PMA in the whole cohort. PAAT:RVET was higher at day 5-7 compared with baseline at birth. There was less than 10% variability in heart rate across the 4 time points (**Tab. 1**). Infants with CLD (n = 129, 59%) had a lower day 2 PAAT when compared with infant without CLD (45 [10] vs. 50 [10], p = 0.005). There was no difference in PAAT values at other time points between infants with and without CLD. There was high intra-observer agreement for PAAT measurement (bias 8%, 95% LOA -9.7 to +9.8; CV 5.4% and inter-observer agreement (bias 7%, 95% LOA -8.8 to +8.7; CV 5.1%), with excellent linear correlation (r = 0.97, p < 0.001 and r = 0.96 p < 0.001 respectively). PAAT:RVET had similar results.

CONCLUSIONS

This study establishes reference values of PAAT in preterm infants and tracks the maturational changes during postnatal development. The study suggests that PAAT can be used as a complementary modality to assess pulmonary hemodynamic function in neonates and facilitates its incorporation into clinical neonatal guidelines.

Table 1 (ABS 19). Assessment of pulmonary hemodynamic function in preterm infants.

	Day 1	Day 2	Day 5-7	36 weeks	p
n	126	127	92	152	
Heart rate	158 (14)	164 (13)[a]	167 (12)[a]	154 (14)	< 0.001
PAAT (ms)	42 (7)	47 (10)[a]	51 (12)[a]	51 (16)[a]	< 0.001
RVET (ms)	155 (18)	161 (23)	163 (31)	193 (23)[a]	< 0.001
PAAT:RVET	0.28 (0.05)	0.30 (0.07)	0.32 (0.09)[a]	0.27 (0.07)	0.007

Values are presented as means (SD). One way ANOVA with repeated measures was used to compare the first four time points. PAAT: pulmonary artery acceleration time; RVET: right ventricle ejection time.
[a]p < 0.01 compared with baseline.

Systemic circulation and cardiac output

ABS 20

LONGITUDINAL CARDIAC CHANGES IN PRETERM INFANTS WITH PROLONGED EXPOSURE TO A PATENT DUCTUS ARTERIOSUS

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INTRODUCTION

A patent ductus arteriosus (PDA) is a common problem in preterm infants. Our local policy recommends early pharmacological treatment if shunt size is large. However, persistence of a PDA was found up to 40% after treatment. A supportive approach was then adopted until spontaneous closure, or surgical closure if failing to thrive and unable to wean off significant respiratory support. Cardiac failure on ultrasound is also reported as an indication for surgical closure, but longitudinal data on progression towards cardiac failure is not available.

PATIENTS AND METHODS

This is a retrospective analysis of prospectively collected data in preterm infants with a persistent PDA beyond 14 days of life after failed pharmacological treatment. Cardiac ultrasounds were performed on postnatal day 3 and then weekly until PDA closure in all infants less than 30 week gestation. Conventional ultrasound parameters included PDA diameter, cardiac sphericity (diameter/length), left atrium volume and left and right ventricular outputs. Speckle tracking analysis provided parameters of volume, myocardial velocities and deformation (strain, strain rate). Left ventricular filling pressure was calculated from the speckle tracking derived early diastolic volume wave divided by early diastolic basal myocardial velocity (Ee' ratio). Data up till 8 weeks postnatal age is reported.

RESULTS

Twenty three preterm infants (median gestational age 26 weeks, range 23 to 29) were analysed. The PDA closed spontaneously at various time points in 17 infants, surgery was performed in 1 and 1 infant died during the study period. Selected data is presented in **Tab. 1**. Shunt size (PDA diameter,

Table 1 (ABS 20). Longitudinal cardiac change in preterm infants with prolonged exposure to a patent ductus arteriosus (PDA).

	Day 3	Day 14	Week 4	Week 6	Week 8	ANOVA
n	23	23	12	7	4	
PDA diameter (mm)	2.2 (0.4)	2.0 (0.3)	2.2 (0.4)	2.2 (0.3)	2.3 (0.5)	0.700
LVO:RVO ratio	1.32 (0.35)	1.34 (0.45)	1.39 (0.41)	1.39 (0.34)	1.17 (0.44)	0.598
FiO_2 (%)	26 (5)	29 (7)	32 (9)	36 (9)	39 (11)	0.036
pCO_2 (mmHg)	45 (10)	56 (7)	62 (12)	66 (10)	67 (14)	< 0.001
Cardiac sphericity	0.58 (0.09)	0.64 (0.06)	0.65 (0.05)	0.66 (0.04)	0.65 (0.05)	0.019
Left atrium volume (ml/kg)	1.1 (0.4)	1.7 (0.6)	1.9 (0.5)	2.1 (0.5)	2.3 (0.6)	< 0.001
End systolic volume (ml/kg)	0.6 (0.2)	1.1 (0.3)	1.3 (0.2)	1.4 (0.4)	1.3 (0.2)	< 0.001
End diastolic volume (ml/kg)	2.0 (0.5)	3.4 (0.7)	3.8 (0.6)	3.9 (0.7)	3.1 (0.3)	< 0.001
Ejection fraction (%)	70 (5)	68 (6)	66 (4)	65 (6)	60 (6)	0.040
Ee' ratio	4.8 (1.6)	7.9 (2.1)	9.3 (3.9)	9.0 (2.7)	8.6 (3.0)	< 0.001

systemic to pulmonary flow ratio) did not change during the study period and respiratory parameters increased. There were no indications of systolic dysfunction with constant strain, strain rate and systolic myocardial velocity (p = 0.913, 0.772 and 0.761). Ejection fraction decreased, but we did not find any absolute systolic function values < 2 SD below the mean considered normal for age. Cardiac shape, atrial volume, ventricular volumes and filling pressure increased till day 14 when it reached a plateau.

CONCLUSIONS

PDA exposure increased cardiac volumes. After 2 weeks of PDA exposure a compensated cardiac physiology was seen with preserved systolic function and increased ventricular filling pressure. Progression towards absolute ultrasound indications of systolic cardiac failure was not seen in any infant, but clinical signs of congestive heart failure were common with prolonged PDA exposure.

ABS 21

NOVEL NON-INVASIVE MEASUREMENTS IN THE ASSESSMENT OF NORMAL CARDIO-VASCULAR ADAPTATION IN TERM & NEAR TERM INFANTS

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INTRODUCTION

Assessing the adequacy of the circulation in neonates is controversial (Stranak et al., 2014), with concern that traditional measures such as blood pressure may not reliably reflect a neonate's perfusion. Advanced techniques such as near infra-red spectroscopy (NIRS) show promise but require specialist interpretation and are not readily available. There is increasing recognition of the potential of functional echocardiography, and emerging evidence for indices derived from pulse oximeter plethysmographic (pleth) traces in monitoring cardiovascular status in the neonate. This study aims to establish normal values and observe trends for these non-invasive bedside measures in healthy neonates.

PATIENTS AND METHODS

This was an observational cohort study of healthy infants > 33 weeks gestational age (w) admitted to a tertiary NICU for special care. For the first three days of life daily consecutive clinical cardiovascular assessments including capillary refill time and blood pressure were performed. These were combined with daily echocardiographic examinations of superior vena cava flow (SVC), right ventricular outflow (RVO) and patency of the ductus arteriosus. Measurements of modified pleth variability index (mPVI) and pulse transit time (mPTT) were derived from oxygen saturation probes placed in the post-ductal position (**Fig. 1** and **Fig. 2**). Data are displayed as median and interquartile range (IQR); statistical analysis was by Kruskal Wallis Test (p-value of < 0.05 = significant).

RESULTS

40 infants with a median gestational age of 35 w (IQR 34-40 w) and birth weight of 2,555 g (IQR 2,065-3,373 g) were included. Data are presented in **Tab. 1**. Median SVC flow (ml/kg/min) decreased

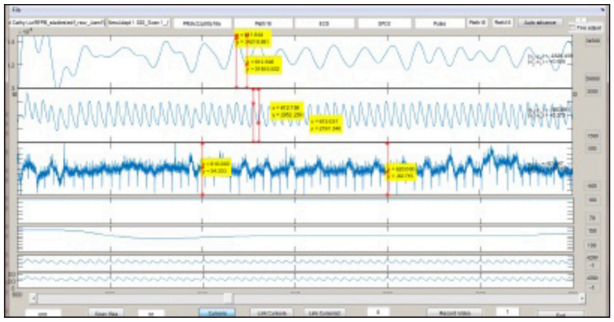

Figure 1 (ABS 21). Graphic depicting modified pleth variability index (mPVI) calculation from raw pleth data.
mPVI is the ratio of the values derived from maximal pleth peaks divided by the minimal pleth peaks over the respiratory cycle.

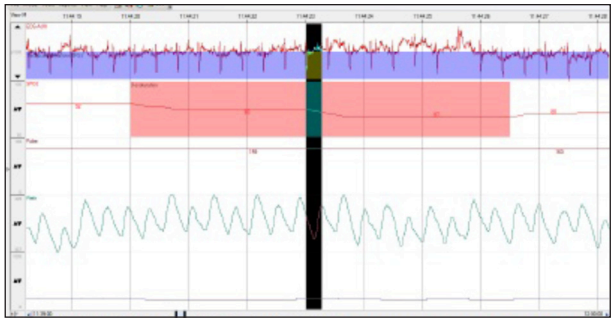

Figure 2 (ABS 21). Graphic depicting modified pulse transit time (mPTT) calculation from raw plethy and ECG data.
mPTT is derived from the time difference between the R wave on the ECG and maximal peak on concurrent raw pleth (as outlined in by the black shading).

Table 1 (ABS 21). Daily research measures. Values are reported as medians and interquartile ranges.

Measurement	Day 1	Day 2	Day 3	p-value[a]	Pairwise comparisons (adjusted p-value)		
					a vs. b	a vs. c	b vs. c
Hour of life taken	21 (12-23)	36 (31-45)	60 (53-69)				
Mean blood pressure (mmHg)	38.5 (38-42)	44.5 (41-48)	54 (43-65)	< 0.0001	0.032	< 0.0001	n.s.
Systolic blood pressure (mmHg)	58 (49-61)	67.5 (60-74)	76 (63-74)	0.0002	0.027	0.0001	n.s.
Diastolic blood pressure (mmHg)	29 (24-31)	32.5 (31-38)	43 (34-56)	< 0.0001	0.02	< 0.0001	n.s.
Heart rate (beat per minute)	129 (118-137)	131 (118-137)	134 (117-146)	0.81	n.s.	n.s.	n.s.
Capillary refill time (seconds)	2 (2-2)	2 (1.9-2.1)	2 (1.9-2.2)	0.93	n.s.	n.s.	n.s.
SpO_2 (%)	99 (97-100)	99 (98-100)	98 (97-99	0.49	n.s.	n.s.	n.s.
SVC volume time integral (cm)	16.5 (14.6-19.5)	15.6 (13.4-19.1)	15 (11.7-20.3)	0.64	n.s.	n.s.	n.s.
SVC diameter (cm)	0.44 (0.39-0.48)	0.43 (0.39-0.49)	0.45 (0.35-0.51)	0.90	n.s.	n.s.	n.s.
SVC flow (ml/kg/min)	158.4 (115.8-187.8)	138.6 (117.3-150.5)	107.2 (86.3-151.1)	0.04	n.s.	0.04	n.s.
RVO volume time integral (cm)	11.9 (10.4-13.4)	11.8 (11.9-13.4)	11.6 (8.7-13.9)	0.85	n.s.	n.s.	n.s.
RVO diameter (cm)	0.787 (0.75-0.86)	0.79 (0.72-0.86)	0.783 (0.68-0.9)	0.86	n.s.	n.s.	n.s.
RVO (ml/kg/min)	321.9 (290.3-366.3)	316.4 (258.3-385.2)	280.3 (202.8-380.2)	0.30	n.s.	n.s.	n.s.
PDA diameter (mm)	0.9 (0-1.9)	0 (0-0.9)	0 (0-0)	0.003	0.04	0.003	n.s.
PDA maximum velocity (m/s)	1.2 (0-2.0)	0 (0-0.2)	0 (0-0)	0.0009	0.01	0.001	n.s.
PDA minimum velocity (m/s)	0.3 (0-1.2)	0 (0-0)	0 (0-0)	0.003	0.03	0.005	n.s.
PVI (%)	21.9 (11.2-28.1)	20.83 (10.2-26.7)	14.3 (8.1-21.9)	0.36	n.s.	n.s.	n.s.
PTT (seconds)	0.29 (0.27-0.29)	0.28 (0.26-0.31)	0.28 (0.26-0.29)	0.67	n.s.	n.s.	n.s.

SVC: superior vena cava flow, RVO: right ventricular outflow; PVI: pleth variability index; PTT: pulse transit time.
[a]From Kruskal Wallis test; n.s.: not significant.

significantly from day 1 (158) to day 3 (107) (p = 0.04). This is in keeping with previous research in uncomplicated infants and is believed to be due to a physiological diuresis after the first 24 hours of life. The decreases in median RVO (321 to 280 ml/kg/min) and mPVI (21.9 to 14.3%) over the first three days of life reflect the normal reduction in pulmonary vascular pressure and vascular resistance over this period of time. Median mPTT values decreased, non-significantly, from 0.29 to 0.28 seconds from day 1 to day 3. PTT is affected by vessel tone and our findings could be explained by the natural increase in peripheral vascular resistance.

CONCLUSIONS

These data provide reference values for plethysmographic measurements of mPVI and mPTT in term and near term infants. These non-invasive biomarkers appear to reflect normal neonatal cardiovascular adaptation, characterised by a decrease in pulmonary and increase in systemic vascular resistance. Further investigation in sick neonates is required to elucidate a potential role

of mPVI and mPTT in the management of the cardiovascular compromise.

ABS 22

PERFUSION INDEX USED AS A SIXTH VITAL SIGN IN PRETERM INFANTS LEADS TO EARLY DIAGNOSIS OF SHOCK AND BETTER OUTCOMES

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INTRODUCTION

Early recognition of shock and preventing fluctuations in systemic blood pressure and cerebral perfusion pressure have been shown to improve neurologic outcomes and survival in prematurity. Maintaining a stable cerebral perfusion pressure or blood pressure is a big challenge in practice. Perfusion index displayed on pulse oxymeter signal has been shown to be a reliable noninvasive indicator of perfusion in adults, with limited data in infants. We studied whether routine inclusion of perfusion index (displayed on pulse oxymetry) as a 6th vital sign documented by nurses will result in overall more stable perfusion status and hence improve outcomes in a busy tertiary referral NICU in India.

PATIENTS AND METHODS

During a 9-month period, premature infants less than 32 weeks gestation were randomly assigned to have perfusion index documented routinely by nurses as a 6th vital sign hourly (test group, n = 93), or not documenting perfusion index routinely by nurses (control group, n = 106). Temperature, heart rate, respiratory rate, blood pressure and SpO_2 were documented hourly in both groups. Poor perfusion was reported to physicians in both groups either based on routine documentation of perfusion index (test group) or picking up based on clinical setbacks or incidental observation (control group). Detailed examination for shock or respiratory events were done by physicians after report of low perfusion index or clinical setbacks. Outcomes in the 2 groups (otherwise similar) were compared.

RESULTS

When shock was identified by routine documentation of perfusion index (test group), severity of shock at the time of diagnosis and need for emergency intubation or resuscitation were significantly less compared to identifying shock by periodic clinical examination or for setbacks (control group).

Need for emergency intubation (near-arrest) at diagnosis of shock: 2/93 in test group, 13/106 in control group.

Lactate > 8 mmol/L before starting inotropes (at diagnosis of shock): 8/93 in test group, 24/106 in control group.

This indicates earlier recognition of shock (before hypotension or severe acidosis) ($p < 0.05$) when perfusion index is routinely, habitually observed by nurses.

The incidence of Grade 3 or 4 intracranial bleeds was much lower in test group: 1/93 in test group, 6/106 in control group, indicating less complications with better monitoring of perfusion.

CONCLUSIONS

Perfusion index used as a 6th vital sign alerts to earlier recognition of shock. It is easier for nurses to observe compared to pulse volume and it is an objective, non-invasive and sensitive parameter for detecting shock. In busy centres, where frequent clinical exam may be compromised, our study shows that sudden life-threatening events and delayed recognition of shock are less likely to occur if perfusion index is included as a 6th vital sign. This may be a neuroprotective strategy.

ABS 23

EARLY CIRCULATORY AND RESPIRATORY PARAMETERS IN EXTREMELY PRETERM INFANTS

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INTRODUCTION

In the last decades improvements in neonatal care have increased survival rates for extremely preterm infants and they constitute a growing population in neonatal intensive care units. To our knowledge there is limited data published on circulatory and respiratory parameters during the first days of life in the most preterm group. A better understanding of the normal physiological changes in early postnatal period may help to more adequately target therapies for circulatory and respiratory complications in this population. Continuous digital monitoring with automatic storing of these parameters gives new possibilities to access and analyze this type of data.

PATIENTS AND METHODS

Infants born before 28 weeks of gestational age (GA) at Uppsala University Children's Hospital between November 2012 and April 2015 were retrospectively identified. Continuous circulatory and respiratory data for the first three days of life was retrieved from a clinical informatics system (IntelliVue Clinical Information Portfolio, Philips) and correlated with baseline data. Arterial blood pressure had been measured in all infants with an indwelling umbilical catheter and blood gases had routinely been drawn from the catheter. Information on respiratory support had manually been registered in the system at least once every hour.

RESULTS

122 infants where born with 9 being excluded from the study because of early death. 33 had a GA of 22-23 weeks, 42 had a GA of 24-25 weeks and 38 had a GA of 26-27 weeks (**Tab. 1**). Heart rate initially decreased in all groups reaching its lowest point in the first postnatal day (**Fig. 1**). Mean blood pressure was constant the first 12 hours in the group with GA 22-23 weeks and increased in the other groups (**Fig. 2**). All infants with GA 22-23 weeks where on ventilator treatment during the first hour of life and 31 (94%) remained on support during the first three days, compared to 41 (96%) and 21 (51%) in the 24-25 weeks group and 28 (78%) and 8 (24%) in the 26-27 weeks group. All groups had a early rise in pO_2 followed by a clear decline during the second part of the first day (**Fig. 3**). pCO_2 decreased during the first hours and then rose steadily during the next day (**Fig. 4**).

Table 1 (ABS 23). Main characteristics of the 113 newborns studied.

	GA 22-23 weeks	GA 24-25 weeks	GA 26-27 weeks
n	33	42	38
Gestational age, weeks (range)	22^{+6} (22^{+0}-23^{+6})	25^{+2} (24^{+0}-25^{+6})	26^{+5} (26^{+0}-27^{+6})
Birth weight, grams (range)	548 (380-840)	712 (387-1,007)	903 (459-1,493)
Male gender (%)	20 (61)	22 (52)	22 (58)
Death (%)	13 (39)	8 (19)	1 (3)

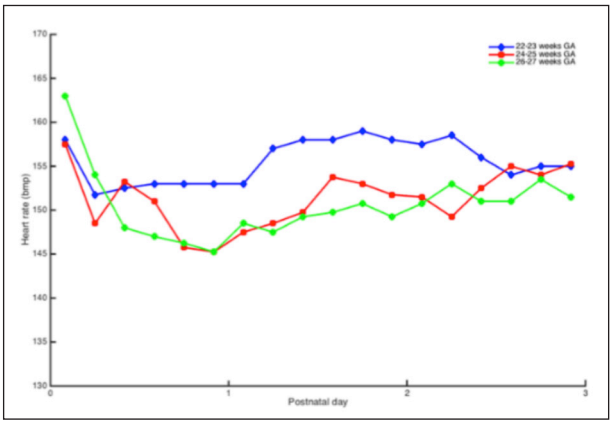

Figure 1 (ABS 23). Heart rates and postnatal days.

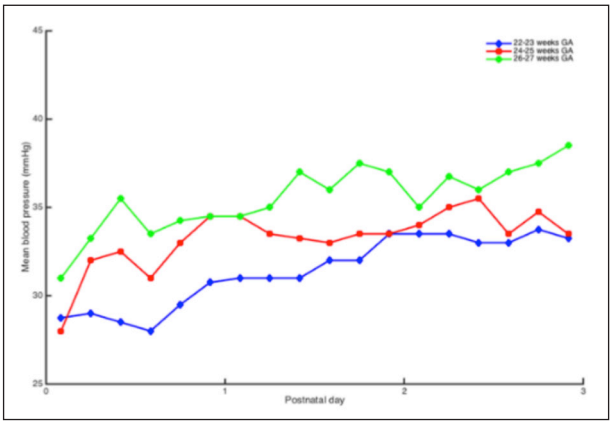

Figure 2 (ABS 23). Mean blood pressure and postnatal days.

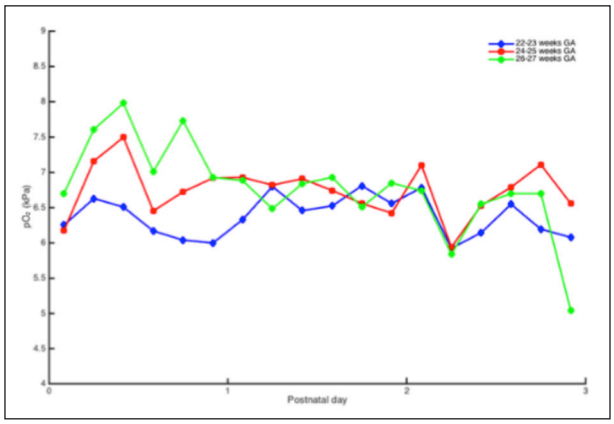

Figure 3 (ABS 23). pO_2 and postnatal days.

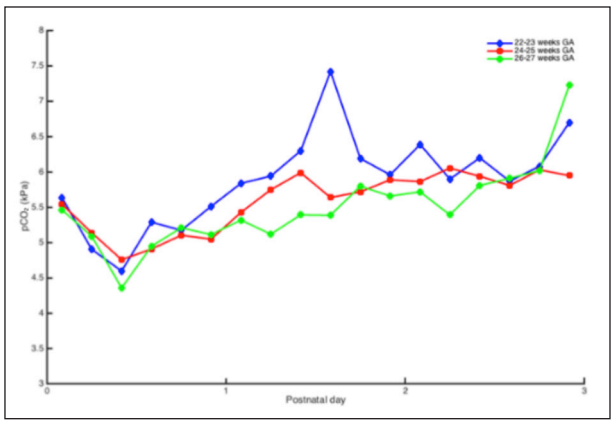

Figure 4 (ABS 23). pCO_2 and postnatal days.

CONCLUSIONS

Circulatory and respiratory parameters are dynamic during the first days of life in extremely preterm infants. Variations in heart rate, blood pressure, pO_2 and pCO_2 likely reflect immense changes in cardiovasculatory function during the transition to postnatal life particularly in the most preterm group. Studies of these parameters could lead to greater understanding and development of therapies for complications related to extreme prematurity.

ABS 24

UK SURVEILLANCE OF SURGICAL LIGATION OF THE PATENT DUCTUS ARTERIOSUS (PDA) IN PREMATURE BABIES PRIOR TO FIRST DISCHARGE HOME

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INTRODUCTION

The first case of surgical ligation of patent ductus arteriosus (PDA) was reported in 1939 in a 7 year old girl. Since then the surgical technique and peri-operative care has advanced a lot. There is still persisting anxiety about the complications related to the surgical ligation. There is no consensus about the ideal timing or patient's characteristics for surgical ligation. The purpose of this study was to describe the peri-operative characteristics of premature infants who undergo surgical ligation of a PDA prior to first discharge home and the complications related to the procedure. We also looked at the current practice in UK.

PATIENTS AND METHODS

A prospective population based survey using the British Paediatric Surveillance Unit (BPSU) was undertaken for 13 months from September 2012. Babies born before 37 completed weeks of gestation, without any other structural cardiac abnormality, who had undergone surgical ligation of a PDA before first discharge home for were looked at. The orange card notification system was used. On notification of a case, a questionnaire was sent to the reporter for data collection. Once this was returned to us, a database was compiled for analysis. Missing data or discrepancies were clarified over the phone for some patients by the team.

RESULTS

We had 270 cases with maximum complete data set in this study. Of these 161 were male. The median gestation was 28.5 weeks and median birth weight was 740 g. The most common reason for referral to surgical ligation was inability to wean respiratory support (81%) and haemodynamically unstable PDA (81%) – **Fig. 1**. On the day prior to surgery 218 were requiring on-going ventilation

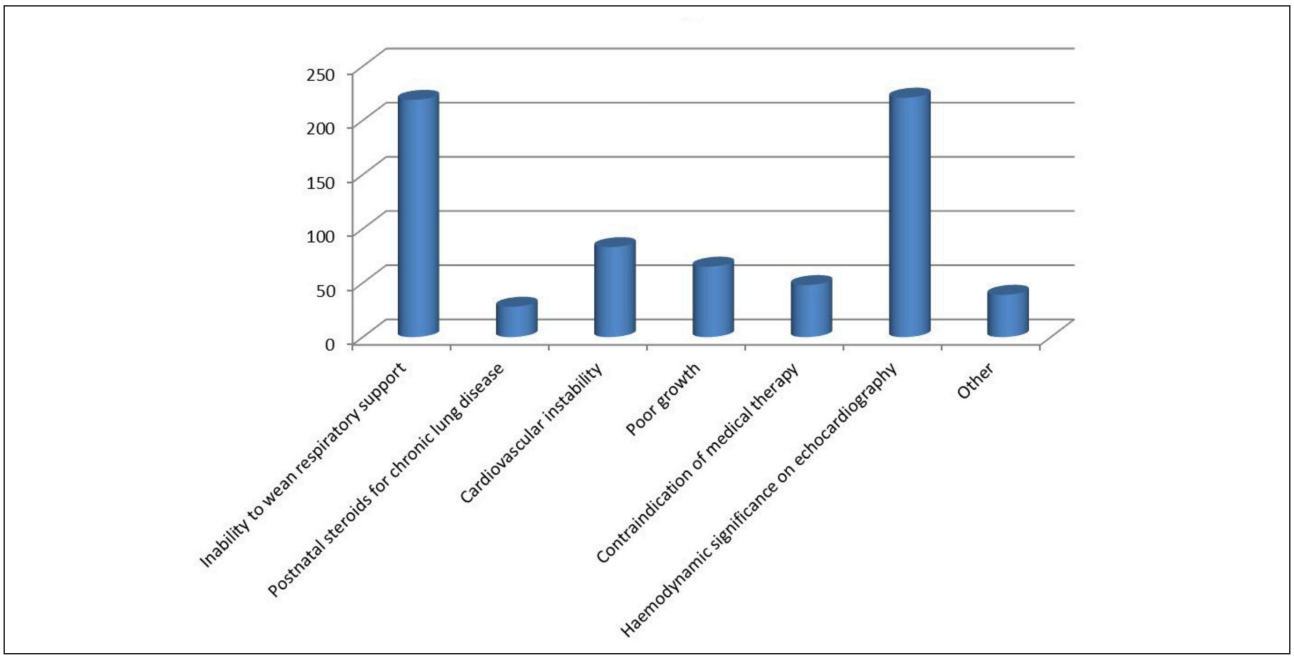

Figure 1 (ABS 24). Reasons of patent ductus arteriosus (PDA) ligation.

(16 were ventilated for transfer), 41 required CPAP and 22 were receiving supplemental oxygen and 4 had no respiratory support. 68% of babies had a trial of medical management including use of NSAIDs prior to surgical ligation. Post ligation, 21% of babies had complications related to surgery, pneumothorax being the commonest. The median age of extubation after surgery was 4 days. 17 babies have been reported to have died in this study although none were related to surgery.

CONCLUSIONS

The practice across UK for surgical ligation of PDA is very varied. ECHO and clinical criteria for haemodynamically unstable PDA is the common reason for referral. Medical and conservative management the duct were used in most of the cases unless contraindicated. One fifth of babies had post-surgical complications. No surgery related deaths have been reported in this group.

ABS 25

CURRENT PRACTICES ON HEMODYNAMIC MONITORING IN NEONATAL INTENSIVE CARE: AN INTERNATIONAL SURVEY

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INTRODUCTION

Monitoring and treatment of a compromised hemodynamic status remains a real challenge in neonatal intensive care patients. Evaluation of the unique aspects of the neonatal developing cardiovascular system requires reliable monitoring systems in order to optimize therapeutic management. In addition to clinical evaluation and blood pressure monitoring, more (advanced) techniques have become available to assess cardiac output, regional blood flow and microcirculation.

PATIENTS AND METHODS

We investigated the current clinical use of (advanced) hemodynamic monitoring systems and the availability of treatment protocols in neonatal intensive care units by using a web-based survey. The 10 questions also addressed the clinical hemodynamic variables used for the assessment and possible subsequent treatment of circulatory failure in the neonate.

RESULTS

79 neonatologists from 28 countries responded. Clinical parameters, invasive blood pressure measurement (frequently used by 78%) and blood gas analysis were regarded the most important parameters for the assessment and possible treatment of poor perfusion. Functional echocardiography (fEcho) was the most commonly used additional method to evaluate circulatory instability (frequently by 42%, sometimes by 37%). NIRS was frequently or sometimes used in 40% for the estimation of end organ perfusion. Other advanced hemodynamic monitoring systems were used mainly in research settings. Fifty-five percent of the respondents indicated to have a protocol for the treatment of neonatal circulatory failure. Availability of protocols differed between regions (Western Europe 83%, Northern Europe 55%, others regions 36%). Treatment recommendations were mainly based on pathophysiology (82%).

CONCLUSIONS

The use of advanced hemodynamic monitoring systems is limited in neonates. Circulatory failure is mainly estimated by clinical signs in combination with blood pressure monitoring. Functional echocardiography is increasingly used but not yet part of standard diagnostic care. When protocols are available, treatment of poor perfusion is based on underlying pathophysiology rather than guided by blood pressure alone.

ABS 26

NON-INVASIVE ASSESSMENT OF DIASTOLIC MYOCARDIAL PROPERTIES IN ELBW NEONATES

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INTRODUCTION

Recent advances in the understanding of heart failure suggest that the impact of diastolic function cannot be ignored. ELBW neonates might be at particular risk for developing diastolic heart failure in view of their immature myocardium. The aim of

this study was to determine values of left ventricular diastolic indices in ELBW neonates during the early postnatal transitional period.

PATIENTS AND METHODS

37 ELBW (GA: 25.4 ± 1.4 weeks, BW: 734 ± 219 g) and 13 term neonates were studied by serial spectral, color-flow and tissue doppler echocardiography on day 1, day 4 and week 3. Mitral inflow velocities (E, A, E/A), mitral inflow propagation velocity slope (Vp), and tissue doppler derived myocardial velocities (medial and lateral mitral E', A', S, IVRT) were determined, and E/E', E/Vp were calculated. The values obtained were also compared with those previously reported for adults.

RESULTS

Mean Vp ($p < 0.001$), E/Vp ($p < 0.001$) values showed a significant decrease over the first 3 weeks of life in ELBW group. Vp values on day 1 (20.5 ± 5.9 cm/s) in ELBW neonates were lower than in term babies ($p < 0.001$) and than those reported in healthy adults. No significant difference found on day 4 and weeks 3 in preterm and term neonates. A positive correlation was found between Vp and cardiac output, LV VTI, but very weak correlation was found between Vp and heart rate and ejection fraction. The mean transmitral E velocity (42.85 ± 9.6 cm/s) and E/A (0.78 ± 0.15) were also lower compared to adults. Myocardial velocities in ELBW neonates were characterized with lower systolic velocities than diastolic ones (LatS: 4.43 ± 0.74 cm/s; LatE': 4.95 ± 0.92 cm/s; LatA': 11.4 ± 1.62 cm/s). In mitral annulus lower E' than A' were found compared to adults.

CONCLUSIONS

The use of Tissue Doppler and Vp are feasible in ELBW neonates. Differences found in echocardiography derived diastolic myocardial properties compared to adults are suggestive for impaired left ventricular relaxation in ELBW neonates. Current approach to hemodynamic management derived from largely adult based experiences may not be ideal for ELBW neonates.

ABS 27

PRIOR CLINICAL DESCRIPTION BIASES ASSESSMENT OF CAPILLARY REFILL TIME

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INTRODUCTION

Capillary refill time (CRT) is a simple clinical measurement used as a component of cardiovascular assessment in neonatal and paediatric patients. Despite known limitations, CRT is widely used to instigate treatment and as a therapeutic endpoint of resuscitation (Surviving Sepsis Campaign, 2012). Although multiple factors are known to affect the reliability of CRT (Fleming et al., 2014) it is used as key part of Early Warning Scores (EWS). No known study has previously explored the relationship between perceived illness severity and CRT estimation. We hypothesised health care professionals (HCPs) assessment of CRT would be biased by perceived level of illness in children.

PATIENTS AND METHODS

Paediatric HCPs were shown 5 video CRT assessments in children. The video clips were analysed digitally to accurately define the CRTs (range 1.7-6 s). Each CRT clip was shown twice, once each with a scenario in the SBAR format where the child was 'well' (EWS low) and once as 'unwell' (EWS high). For comparison, a 1.7-s CRT clip was repeated with a new 'well' and 'unwell' scenario. The video CRTs and corresponding scenarios were randomised (total of 12) and HCPs asked to score the CRT as 1 s intervals (e.g. < 2 s, < 3 s, etc.). Wilcoxon matched-pairs sign rank test was used to calculate differences in response between well and unwell scenarios. Ethical approval was given.

RESULTS

75 paediatric HCP's (33 doctors, 39 nurses, 3 other) participated. No significant differences in responses scoring < 2 s were found for the 1.7-s clip with similar scenarios (well 97% vs. 96%, $p = 0.39$, unwell, 81% vs. 83%, $p = 0.68$). For each CRT length, changing the scenario from a well to an unwell child resulted in significantly different responses to the same recorded CRT length which in a clinical setting could have resulted in over or under treatment in four out of the five scenarios (**Tab. 1**).

CONCLUSIONS

This study suggests that HCPs assessment of CRT is biased by prior clinical knowledge of the patient, and may explain why it performs well in previous studies in identifying a sick baby or child. A more objective way of measuring CRT could increase its accuracy and reliability making a more useful clinical assessment tool of cardiovascular status in babies and children.

Table 1 (ABS 27). Clinical significance of responses given as percentages. Shaded boxes indicate correct category for capillary refill time (CRT).

CRT (seconds)	Responses (%)									
	1.7 (n = 150)		2.2 (n = 75)		2.4 (n = 75)		4.9 (n = 75)		6 (n = 75)	
	W	U	W	U	W	U	W	U	W	U
≤ 2 s	97	82	97	96	72	47	8	4	16	4
> 2 s	3	18	3	4	28	54	92	96	84	96
p-value	< 0.0001		0.0257		0.0004		< 0.0001		< 0.0001	

ABS 28

AFTERLOAD REDUCTION IN CATECHOLAMINE-RESISTANT SHOCK IN EXTREME PREMATURITY: NOVEL THERAPY WITH OLD DRUG FOR AN UNRECOGNIZED FACTOR IN SHOCK

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INTRODUCTION

High systemic vascular resistance (SVR) is a common, but under-recognized association of shock in extreme prematurity. In these cases, poor tissue perfusion (acidosis, oliguria, poor sensorium, etc.) persisting after achieving so-called "normal blood pressures" is difficult to diagnose and manage. High SVR may be intrinsic after removing placenta or inotrope-induced. Afterload reducers have not been well studied in this population (unlike older ages), except a few reports of milrinone use. We examined the role of nitroglycerin (NTG) in catecholamine-refractory shock in extreme prematurity in a large referral NICU, as it is cheaper, more convenient to use than milrinone.

PATIENTS AND METHODS

Subjects

23 preterm neonates (< 30 weeks gestation) with persistent shock due to sepsis or asphyxia (cold extremities, weak pulses, lactic acidosis, oliguria, low or normal BP) persisting after 2 hours of:

- adequate fluid-resuscitation (good IVC filling after fluid boluses)
- adequate inotrope therapy stepped up as per standard protocols (10 mcg/kg/min of dobutamine, dopamine and 0.3 mcg/kg/min of epinephrine infusions).

Intervention

NTG infusion at 2.5 to 5 mcg/kg/min was added after achieving at least low normal mean blood pressure (equal to gestational age in weeks minus 3), continued for 72 h, and titrated to maintain BP (exclusion criteria: refractory hypotension, warm shock). ECHO showed ejection fraction < 45% in 8/23 infants while starting NTG.

RESULTS

Effectiveness of NTG is shown in **Tab. 1**. Within an hour after starting NTG, pulse volume, serum lactate, urine output and ejection fraction improved, and this effect was pronounced by 4 hours ($p < 0.05$). Improvement in shock was more dramatic with addition of NTG, compared to use of inotropes only. There were no adverse effects of NTG.

CONCLUSIONS

This study emphasizes the need to study afterload reduction in selected cases of shock in extreme preterms. Increased SVR is an important component of shock in premature infants, but under-recognized. In addition to augmenting myocardial contractility and optimizing blood pressures with inotropes, afterload reduction will

Table 1 (ABS 28). Effect of nitroglycerin (NTG) in shock.

n = 23	0 h start of NTG	1 h after starting NTG	4 h after starting NTG
pulse volume	+/-	+/++	++
mean serum lactate (mmol/L)	8.7	5.7	3.6
mean urine output (ml/kg/hr)	0.7	1.2	2.3
mean ejection fraction	54%		59%

improve tissue perfusion and decrease stress on myocardium. NTG is effective for this on the basis of our study.

ABS 29

HEART FUNCTION ASSESSMENT IN ASPHYXIA; SPECKLE TRACKING ECHOCARDIOGRAPHY PERFORMS BETTER THAN TISSUE DOPPLER ECHOCARDIOGRAPHY AND FRACTIONAL SHORTENING

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INTRODUCTION

Strain and strain rate indices of heart function can be obtained by speckle tracking echocardiography (STE) by 2D strain and by tissue Doppler echocardiography (TDE). STE analyses are faster and easier to perform, but validation against other indices in neonates are scarce. The aim of this study was to compare heart function indices by STE and by TDE between non-asphyxiated and asphyxiated neonates.

PATIENTS AND METHODS

The heart function indices peak systolic strain, peak systolic strain rate, early diastolic strain rate and strain rate during atrial contraction were obtained serially on day 1 and 3 of life in neonates by STE and by TDE. Apical 4-chamber images were used. All indices were averaged over three consecutive heart cycles. The left ventricle STE indices were assessed from analysis of the septum and left lateral wall combined. The right heart STE indices were assessed from the right lateral free wall. The left and right heart indices were averaged into STE indices for each examination. The TDE indices from each examination were averaged from one large segment in the left lateral wall, the septum and the right lateral wall. Measurements from day 1 and day 3 were averaged.

RESULTS

Forty-eight non-asphyxiated term neonates (5 min Apgar score, median: 9, range: 8-10) and 20 asphyxiated term neonates (5 min Apgar score, median: 5, range: 4-6) were included. Asphyxiated neonates were treated at normothermia. All STE indices except the peak systolic strain rate were significantly lower in the asphyxiated neonates ($p < 0.05$). The peak systolic strain and the strain rate during atrial contraction by TDE were lower in the asphyxiated neonates ($p < 0.05$) while the peak systolic strain rate and early diastolic strain rate by TDE were not (**Fig. 1**). The fractional shortening was similar between the groups.

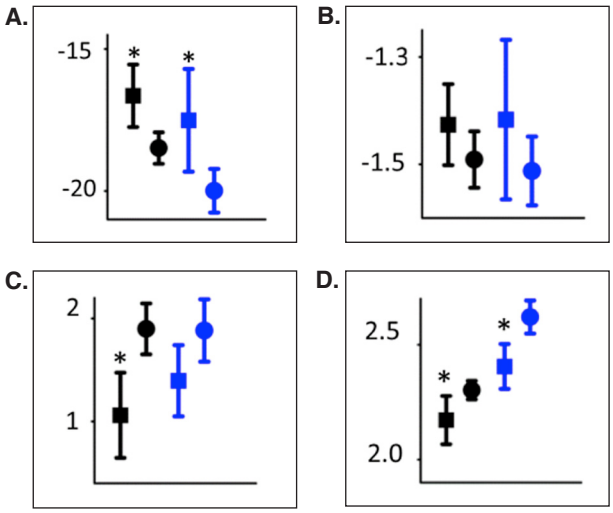

Figure 1 (ABS 29). A. Peak systolic strain (%). **B.** Peak systolic strain rate (/s). **C.** Early diastolic strain rate (/s). **D.** Strain rate during atrial contraction (/s).

Mean and 95% CI. Black bars: speckle-tracking indices; blue bars: tissue Doppler indices; squares: asphyxiated neonates; circles: non-asphyxiated neonates; *significantly different from non-asphyxiated neonates ($p < 0.05$).

CONCLUSIONS

Speckle tracking indices performed better than fractional shortening and tissue Doppler indices for assessing the reduced heart function in asphyxiated neonates. Tissue Doppler indices were less sensitive than speckle tracking indices and more sensitive than fractional shortening for assessing the differences.

ABS 30

GLOBAL RIGHT VENTRICULAR FRACTIONAL AREA CHANGE IS A SURROGATE MARKER FOR SYSTEMIC BLOOD FLOW IN PRETERM INFANTS

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INTRODUCTION

Estimating systemic blood flow (SBF) in preterm infants is a challenge. Global right ventricular fractional area change (RV FAC) represents RV ejection fraction; it is highly dependent on systemic venous return and may reflect SBF. We aimed to: (1) assess the relationship between RV FAC and left ventricular output (LVO) at 10 hours of age when the patent ductus arteriosus (PDA) is not haemodynamically significant; (2) assess the impact a haemodynamically significant PDA (hsPDA) has on RV FAC at day 6 of age; and (3) assess the relationship between a low RV FAC at 10 hours of age and the evolution of severe intraventricular haemorrhage (IVH) by the first week of age.

PATIENTS AND METHODS

Preterm infants < 29 weeks gestation underwent echocardiography assessments at 10 hours and 6 days of age. PDA treatment was not carried out during the study period. RV FAC was measured from focussed RV four- and three-chamber views. LVO, PDA diameter and peak velocity (V_{max}), descending aortic diastolic flow, and flow across the patent foramen ovale (PFO) were assessed. A hsPDA was defined as a PDA with reversed diastolic flow in descending aorta. A cranial ultrasound was carried out on all infants on day 6 of age. Severe IVH was defined as IVH grade 3 and 4.

RESULTS

102 infants with mean (SD) gestation and birthweights of 26.5 ± 1.4 wks and 965 ± 237 grams were prospectively enrolled. All infants had a PDA with a mean diameter of 2.4 ± 0.6 mm and mean V_{max} of 1.2 ± 0.6 m/s but none had descending aortic flow reversal at 10 hours. There was a significant positive correlation between RV FAC and LVO (r = 0.5, p < 0.001, **Fig. 1**). On day 6, there was an increase in PDA diameter (2.7 ± 0.7 mm, p = 0.03) and an increase in the V_{max} (2.0 ± 0.8 m/s, p < 0.001) and the correlation between RV FAC and LVO was lost (r = -0.2, p = 0.1). RV FAC was lower in infants with hsPDA (n = 35) at day 6 compared to those without hsPDA (43 ± 6% vs. 48 ± 7%, p = 0.005). RV FAC at 10 hours of age was lower in infants developing severe IVH by the first week of life (29 ± 8% vs. 35 ± 9%, p = 0.03). All those relationships remained significant when adjusting for the shunt across the PFO.

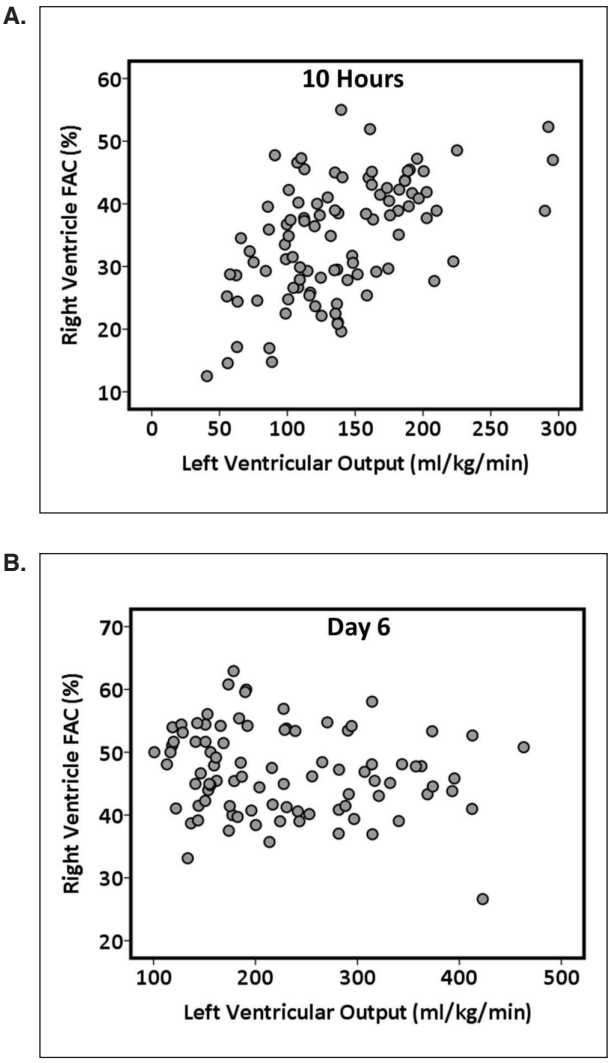

Figure 1 (ABS 30). Correlation between right ventricular fractional area change (RV FAC) and left ventricular output (LVO) at 10 hours (**A**) and on day 6 (**B**).

CONCLUSIONS

RV FAC may be a surrogate marker for systemic blood flow in the presence or absence of a hsPDA. The presence of a PFO did not affect this relationship suggesting that the shunt across the PFO is not of a large volume.

ABS 31

HEART RATE VARIABILITY CHANGES ASSOCIATED WITH NEONATAL INFECTION

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INTRODUCTION

It has been reported that the Heart Rate Characteristic (HRC) index may be useful in predicting sepsis in newborn infants more than 1 week after birth (Griffin et al., Pediatric Research. 2007;61:222-7). The aim of this study was to examine if visual review of Heart Rate Variability (HRV) might detect changes associated with early onset of infection.

PATIENTS AND METHODS

Physiological data (heart rate, respiratory rate and SpO_2) were acquired from preterm infants undergoing varying levels of intensive care treatment. The data were collected using standard cotside monitors (GEC Solar) which downloaded automatically at one minute intervals into MetaVision, a patient electronic record (iMDsoft®, Israel). Data were exported from MetaVison to spreadsheet files and the recordings were randomised. The minimum recording length for inclusion was 15 hours. We developed software using MATLAB® (The MathWorks Inc., USA) in order to display heart rate changes in sections of 5 hours; for each recording heart rate was assessed visually as being either of normal variability or of low variability.

RESULTS

Data were analysed on 15 infants with suspected infection. Nine infants had positive bacterial blood cultures and one had positive bacterial cultures from a wound swab. The median (range) gestation at birth was 26 (24-30) completed weeks. The segments of data analysed commenced from a median (range) age of 20 (0-77) days. For 14 babies two data periods were analysed. The first just prior to clinically identified infection or CRP rise and the second with clinical signs of sepsis and a CRP rise. 8 of 9 recordings in babies with positive blood cultures had low HRV (**Fig. 1**) and of 6 infants without positive blood cultures all had normal HRV (**Fig. 2**); low HRV had a sensitivity of 89% for concurrent positive bacterial blood cultures. Furthermore 15 of 20 recordings prior to clinically identified infection or in babies without proven bacterial sepsis had normal HRV.

CONCLUSIONS

The results of this study suggest that a simple display of heart rate variation over several hours may allow early identification of infants at risk of developing infection. Further studies are required to investigate how the start of reduced HRV might be related to the onset of infection.

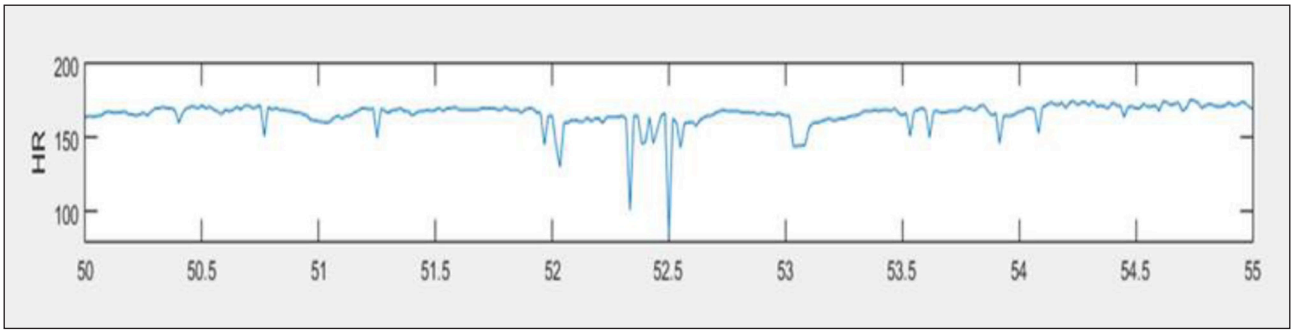

Figure 1 (ABS 31). Low Heart Rate Variability (HRV) .

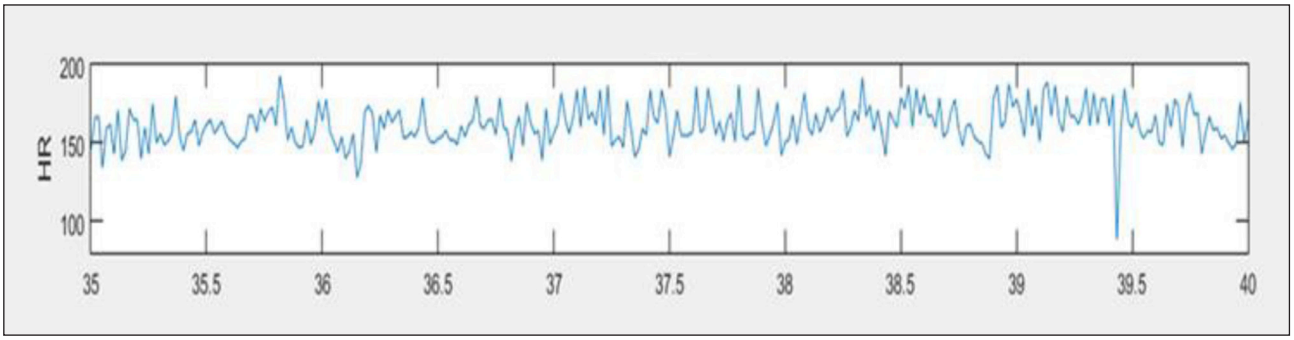

Figure 2 (ABS 31). Normal Heart Rate Variability (HRV) .

ABS 32

POINT OF CARE FUNCTIONAL ECHOCARDIOGRAPHIC INTER- AND INTRA-OBSERVER VARIABILITY: RIGHT VENTRICULAR OUTFLOW & SUPERIOR VENA CAVA FLOW IN WELL AND UNWELL NEWBORN INFANTS

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INTRODUCTION

Functional echocardiography has been recommended as a bedside method of gaining useful clinical information on neonatal cardiac function and systemic perfusion, and it may help guide treatment. There has been debate in the literature on the accuracy of measures such as superior vena cava (SVC) flow and right ventricular outflow (RVO), particularly with regard to their intra- and inter-observer variability. Much of the prior literature has focused on extremely preterm infants or well term or near term infants. We present data on the variability of these echocardiographic measures in well and unwell near term infants admitted to a single tertiary neonatal unit.

PATIENTS AND METHODS

Data were collected as part of prospective observational cohort studies including babies who were healthy, or receiving intensive care or total body cooling, 33 weeks gestation. Enrolled infants underwent daily echocardiograms for the first three days of life, including SVC flow and RVO assessments as described previously by Osborn & Evans (2002). Intra-observer measurements were performed 10 minutes apart from each other by one observer. Inter-observer measurements were taken by two mutually blinded observers, one immediately after the other. Variability was analysed using Wilcoxon rank test and Bland Altman plots (see picture). Median results and interquartile ranges (IQR) are reported (**Tab. 1**) with p-values less than < 0.05 considered significant.

Table 1 (ABS 32). Showing measures included in the intra- and inter-observer variability analysis.

Intra-observer				
Intra-observer measure	**Measurement 1**	**Measurement 2**	**Variability of the median value**	**Wilcoxon Rank Sign Test (p =)**
SVC diameter (cm)	0.52 (0.42-0.61)	0.50 (0.41-0.60)	5.1% (3.1-9.9%)	
SVC volume time integral (cm)	14.64 (11.85-16.79)	13.76 (11.97-16.29)	9.2% (3.9-16.2%)	
SVC heart rate (beats per minute)	118 (106-135)	119 (105-140)	5.4% (1.3-7.9%)	
SVC flow (ml/kg/min)	117.7 (75.9-173.1)	125.5 (74.8-154.7)	17.1% (8.7-32.1%)	0.53
RVO diameter (cm)	0.86 (0.72-0.90)	0.83 (0.74-0.94)	4.1% (2.0-5.7%)	
RVO volume time integral (cm)	10.51 (9.16-11.90)	10.09 (8.90-12.90)	9.3% (4.2-13.5%)	
RVO heart rate (beats per minute)	122 (106-131)	122 (103-131)	4.8% (1.7-10.4%)	
RVO flow (ml/kg/min)	252.8 (203.2-333.9)	245.2 (181.9-329.8)	9.7% (4.9-22.5%)	0.93
Inter-observer				
Inter-observer measure	**Observer 1**	**Observer 2**	**Variability of the median value**	**Wilcoxon Rank Sign Test (p =)**
SVC diameter (cm)	0.44 (0.42-0.54)	0.44 (0.38-0.49)	7.0% (0.9-10.4%)	
SVC volume time integral (cm)	15.11 (12.52-16.20)	14.39 (12.64-17.83)	11.0% (5.4-13.9%)	
SVC heart rate (beats per minute)	117 (103-132)	116 (105-141)	5.8% (1.5-7.3%)	
SVC flow (ml/kg/min)	115.9 (84.9- 156.2)	113.5 (71.2-156.5)	10.2% (5.6-22.1%)	0.19
RVO diameter (cm)	0.84 (0.75-0.88)	0.81 (0.71-0.89)	6.7% (5.0-14.4%)	
RVO volume time integral (cm)	10.48 (9.3- 11.9)	10.39 (8.60- 11.65)	8.9% (4.9-13.9%)	
RVO heart rate (beats per minute)	116 (108-134)	124 (106-141)	6.1% (0.0-8.9 %)	
RVO flow (ml/kg/min)	243.1 (188.1-303.7)	193.9 (148.7-327.4)	24% (13.7-37.0%)	0.73

Values are reported as medians and interquartile ranges.

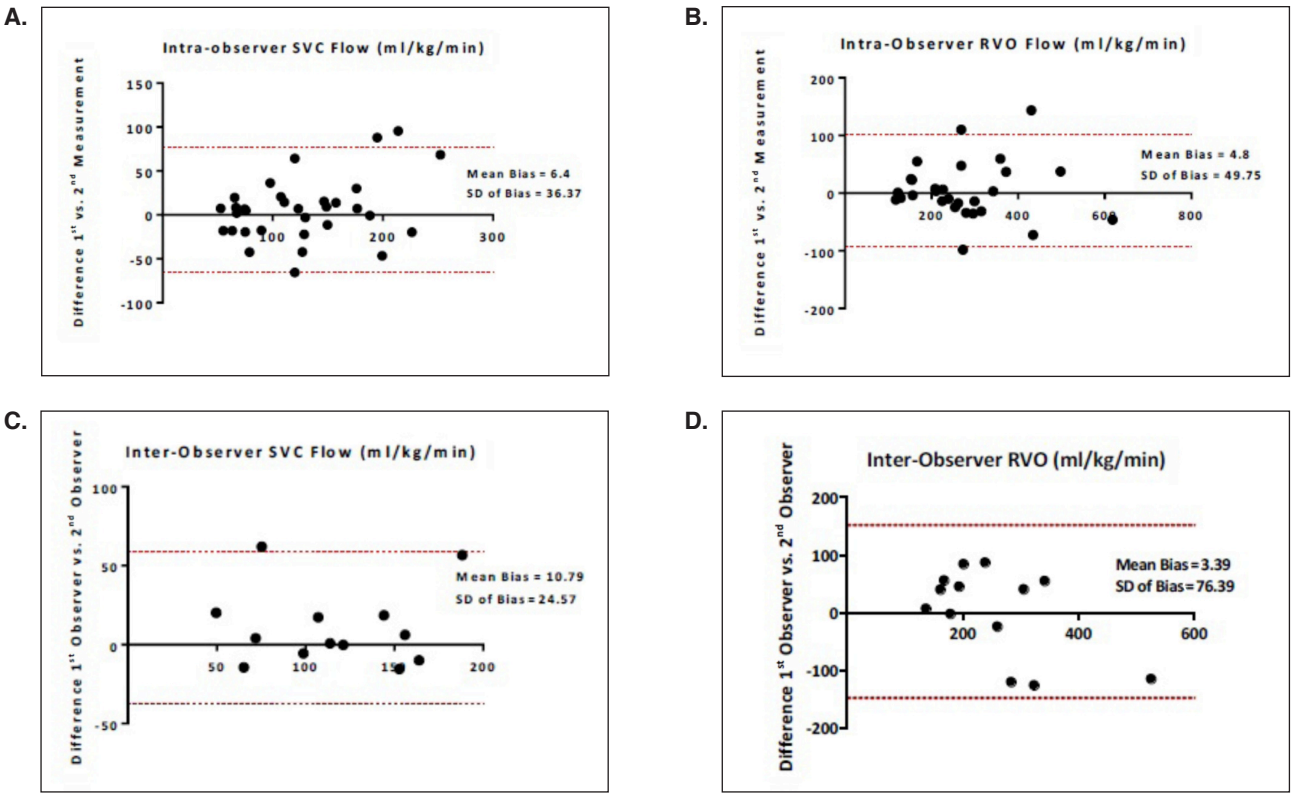

Figure 1 (ABS 32). A, B. Intra-observer superior vena cava (SVC) flow and right ventricular outflow (RVO). **C, D.** Inter-observer superior vena cava (SVC) flow and right ventricular outflow (RVO).

RESULTS

Results are presented in **Fig. 1**. For the intra-observer analysis, 32 infants with median gestational age 38 weeks (IQR 34-40) and birth weight 3,098 g (1,995-3,953 g) were studied. There was no significant difference between the intra-observer SVC flow (117 vs. 125 ml/kg/min; p = 0.53) or RVO measurements (252 vs. 245 ml/kg/min; p = 0.26). The intra-observer variability for the median values of the measurements gained was 17.1% and 9.7% respectively. For the inter-observer analysis, 13 infants with median gestational age 36 weeks (34-40) and birth weight 2,815 g (2,228-3,530 g) were studied. There was no significant difference between the inter-observer SVC flow (115 vs. 113 ml/kg/min; p = 0.19) or RVO measurements (243 vs. 193 ml/kg/min; p = 0.73). The inter-observer variability for the median values gained was 10.2% and 24% respectively.

CONCLUSIONS

We found no significant differences between either intra- or inter-observer measurements of either RVO or SVC flow; the variability the median values and bias are widely dispersed but are within acceptable limits in this population of neonates. This study indicates that SVC flow and RVO are robust bedside echocardiographic measures of systemic blood flow in neonates who are healthy, requiring intensive care or total body cooling.

Transfusion and volume therapy

ABS 33

UK TRANSFUSION-ASSOCIATED NECROTISING ENTEROCOLITIS CASES IDENTIFIED THROUGH A MULTICENTRE AUDIT

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INTRODUCTION

Transfusion-associated necrotising enterocolitis (TANEC) has been reported from The Americas and various European countries at rates comprising 27-38% of necrotising enterocolitis (NEC) cases. Compared with overall NEC cases, babies with TANEC have typically been born at earlier gestations, had at least one prior packed red blood cell (PRBC) transfusion, and are aged 3-5 weeks postnatal at NEC onset. While the role of PRBC transfusion in causation of NEC remains debated, there are surprisingly few reports of TANEC in the UK setting. Our aims were to evaluate using uniform definitions the incidence of TANEC in UK NICUs and to assess the characteristics of cases.

PATIENTS AND METHODS

We undertook a retrospective, collaborative, multicentre audit of NEC cases in very low birth weight (VLBW) infants occurring in four tertiary-level UK NICUs during the period October 2011 to November 2014. We assessed whether definite NEC cases (NEC diagnosed surgically via laparotomy, post-mortem, and/or a strict clinical-radiological diagnosis) were also TANEC cases (first onset of NEC symptoms within 48 hours of commencement of a PRBC transfusion). For each identified TANEC case we used a detailed data collection proforma to record characteristics. Of the participating NICUs, three introduced routine probiotic prophylaxis during the study period and one practised routine cessation of enteral feeding during PRBC transfusions.

RESULTS

1,608 (20.1%) of 8,007 babies admitted in the 38-month study period were VLBW and 68 (4.2%) had definite NEC. Of these 15 (22.1%) were TANEC; 34 (50.0%) had received prior PRBC transfusion but were not TANEC; 19 (27.9%) had received no prior PRBC transfusion. Across NICUs, the incidence of definite NEC ranged from 4.5-9.7 cases/year (3.6-7.8 per 100 VLWB admissions) and that of TANEC ranged from 0.50-1.95 cases/year (0.4-1.7 per 100 VLWB admissions). The proportion of TANEC/NEC cases within individual NICUs ranged from 11-40%. Four (27%) TANEC cases occurred in babies who had received prior prophylactic probiotics. **Tab. 1** shows the baseline characteristics of TANEC cases.

CONCLUSIONS

TANEC occurs in the UK in proximal association with PRBC transfusion at rates similar to those reported from other countries. Rates of NEC and TANEC cases varied widely between our UK centres. In common with reports from elsewhere, the UK TANEC cases were compromised of lowest gestation babies although age at onset varied widely. A large prospective UK surveillance study is now indicated to improve the understanding of the causation of TANEC.

Table 1 (ABS 33). Baseline and transfusion characteristics of the 15 transfusion-associated necrotising enterocolitis (TANEC) cases.

Gestational age at birth, weeks	25^{+1} (23^{+2} to 27^{+0})
Birth weight, g	695 (527-1,070)
Male	5 (33%)
Small for Gestational Age	4 (27%)
Confirmed PDA within < 2 weeks prior	7 (47%)
Ibuprofen treatment given < 2 weeks prior	3 (20%)
Proven sepsis within < 1 weeks prior	5 (33%)
Receiving at least half of feeds enterally at TANEC onset	12 (80%)
Received any probiotics prior to TANEC	4 (27%)
Surgical intervention needed	12 (80%)
Survived to discharge	9 (60%)
PRBC transfusions given prior to NEC onset (including index transfusion), n	4 (1 to 14)
Age at start of index PRBC transfusion, days	18 (0 to 69) [IQR: 5-36]
Main reason for index PRBC transfusion:	
Routine top up	9 (60%)
Symptomatic anaemia	3 (20%)
Not specified	3 (20%)

Data are median (range) or n (%).
IQR: interquartile range.

ORAL COMMUNICATIONS

ABS 34

LONGITUDINAL ASSESSMENT OF MYOCARDIAL STRAIN AND STRAIN RATE AND THE EFFECT OF CHRONIC LUNG DISEASE IN PRETERM INFANTS LESS THAN 29 WEEKS GESTATION

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INTRODUCTION

There is a lack of longitudinal data on left ventricular (LV) septal and right ventricular (RV) tissue-Doppler derived strain, systolic and diastolic strain rate in preterm infants less than 29 weeks gestation. In addition, data on RV-specific function parameters such as tricuspid annular plane systolic excursion (TAPSE) and global RV fractional area change (FAC) warrant further study. We aimed to describe the change in those parameters over the first week of life and at 36 weeks corrected gestational age, examine the influence of various early haemodynamic markers and examine the influence of chronic lung disease (CLD) on those parameters.

PATIENTS AND METHODS

This was a prospective study of markers of increased LV preload (pulmonary vein Diastolic wave, PVd) during days 5-7. The difference in parameters between infants with and without CLD at 36 weeks corrected gestation was evaluated.

RESULTS

105 infants with a mean (SD) gestation and birthweight of 26.9 (1.4) weeks and 979 (234) grams were included. Echocardiography data was available for all infants on days 1 to 5-7 and for 47 infants at 36 weeks. There was an increase in most of the parameters across the four time points (**Tab. 1**). On day 1, there was a negative correlation between SVR and LV strain (r = -0.3, p = 0.01), SVR and septal strain (r = -0.4, p 1.5 mm has higher LV strain

Table 1 (ABS 34). Echocardiographic parameters across the four time points.

	Day 1	Day 2	Day 5-7	36 weeks	p-value
Left ventricle					
Strain (%)	-12.2 (2.8)	-12.2 (2.8)	-12.7 (2.2)	-15.0 (2.2)[a]	< 0.001
Systolic SR (1/s)	-1.5 (0.5)	-1.7 (0.6)[a]	-1.7 (0.5)[a]	-1.8 (0.5)[a]	0.02
Early diastolic SR (1/s)	1.6 (0.8)	2.1 (0.6)	2.1 (0.7)	2.1 (0.9)	0.2
Late diastolic SR (1/s)	2.6 (0.8)	2.7 (1.0)	2.7 (0.9)	3.2 (1.2)	0.08
Septum					
Strain (%)	-15.5 (3.0)	-17.4 (3.5)[a]	-17.9 (3.1)[a]	-20.6 (3.6)[a]	< 0.001
Systolic SR (1/s)	-1.6 (0.3)	-1.9 (0.4)[a]	-2.0 (0.4)[a]	-2.1 (0.4)[a]	< 0.001
Early diastolic SR (1/s)	1.7 (0.6)	2.1 (0.6)[a]	2.1 (0.7)[a]	2.0 (0.6)	0.001
Late diastolic SR (1/s)	2.3 (0.8)	2.7 (1.0)[a]	2.7 (0.9)[a]	2.7 (1.0)[a]	0.03
Right ventricle					
Strain (%)	-22.8 (4.8)	-24.3 (4.7)[a]	-25.1 (4.9)[a]	-28.0 (5.5)[a]	0.001
Systolic SR (1/s)	-2.1 (0.5)	-2.5 (0.7)[a]	-2.9 (0.7)[a]	-3.0 (0.7)[a]	< 0.001
Early diastolic SR (1/s)	2.4 (0.8)	2.6 (0.7)	2.7 (0.9)	2.9 (0.9)	0.4
Late diastolic SR (1/s)	3.6 (1.0)[a]	4.4 (1.3)[a]	4.3 (1.3)[a]	4.6 (1.6)[a]	0.008
nTAPSE (mm)	2.6 (0.6)[a]	3.1 (0.6)[a]	3.3 (0.5)[a]	3.9 (0.7)[a]	< 0.001
Global FAC (%)	34 (9)[a]	43 (7)[a]	47 (7)[a]	48 (6)[a]	< 0.001

Values are presented as means (SD). P-values represent one way repeated measures ANOVA.
[a]p-value < 0.05 compared with baseline Day 1 values.

(-13.0 [2.4] vs. -11.9 [1.9], p = 0.03). There was a positive correlation between PVd and LV strain (r = 0.3, p = 0.002) and PVd and septal strain (r = 0.3, p = 0.01). At 36 weeks, infants with CLD (n = 28/47) had lower RV strain (-26.4 [5.0] vs. -30.7 [5.5], p = 0.0.1), lower RV SRa (4.2 [1.3] vs. 5.3 [1.9], p = 0.04), and lower normalised TAPSE (3.7 [0.6] vs. 4.2 [0.7], p = 0.03).

CONCLUSIONS

Myocardial function measured using tissue-Doppler derived deformation parameters, TAPSE and FAC undergo important longitudinal changes in preterm infants. Left heart strain measurements in preterm infants appear to be influenced by changes in preload and afterload. CLD appears to negatively impact RV function.

ABS 35

THE EFFECT OF PRENATAL CAFFEINE ON THE CARDIOVASCULAR TRANSITION AT BIRTH

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INTRODUCTION

Caffeine is commonly used to treat apnea in preterm infants, but little is known about its effects on cardiovascular changes during transition from fetal to neonatal life. As caffeine is routinely given to infants hours after birth, in view of it's success, earlier administration in the delivery room is being considered. We hypothesise that a caffeine administration to the infant prior to birth will not only stimulate breathing, but also will increase heart rate and blood pressure, particularly after cord clamping (CC).

Our aim was to determine the effects of prenatal caffeine infusion on cardiovascular function and pulmonary blood flow during transition in preterm lambs.

PATIENTS AND METHODS

This is a prospective intervention study using a preterm lamb model. Preterm lambs (~125 days of gestation; term 147 days) underwent surgery, to instrument with catheters (carotid artery and jugular vein) and transonic flow probes (pulmonary artery and carotid artery), immediately before delivery by caesarean section. Before the cord was clamped, lambs were intubated and a caffeine (10 mg/kg caffeine-base) or saline infusion was infused intravenously into the ewe and lamb over a 15-minute period. Two minutes after clamping the cord, ventilation commenced with a sustained inflation (35 cmH_2O for 30 seconds) followed by ventilation for 30 minutes (target tidal volume of 6-8 ml/kg).

RESULTS

Median (range) systolic (71 mmHg [61-71] vs. 59 mmHg [54-61], p < 0.001), diastolic (51 mmHg [46-52] vs. 45 mmHg [39-46], p < 0.001) and mean carotid blood pressure (57 mmHg [51-58] vs. 50 mmHg [44-51], p < 0.001) were markedly higher in the caffeine treated group over the first 10 heartbeats after CC. Median pulmonary blood flow over the first 10 heartbeats after CC was significantly increased in the caffeine group (91 ml/min [61-95] vs. 65 ml/min [50-68], p < 0.001). The median carotid blood flow, however, was lower in the caffeine group than in the saline group (127 ml/min [102-132] vs. 136 ml/min [117-139], p = 0.005).

CONCLUSIONS

These data show that heart rate, pulmonary blood flow and carotid blood pressure increase in response to caffeine infusion, possibly due to peripheral vasoconstriction.

ABS 36

FEASIBILITY OF USING THE ELDON CARD IN THE PERIPARTUM DIAGNOSIS OF RH INCOMPATIBILITY BETWEEN MOTHERS AND THEIR NEWBORNS

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INTRODUCTION

Hemolytic Disease of the Foetus/Newborn (HDFN) occurs when a Rhesus (Rh) negative woman, previously sensitised to the Rh D antigen in a pregnancy with an Rh positive baby, carries another Rh positive

baby in a later pregnancy. It is preventable if the blood groups of the mother and baby are known early so that appropriate management is started. Universal blood group testing is an issue in developing countries like Ghana, hence the persistence of the disease. The Eldon Card is a point of care method of ABO-Rh group testing which has been used by armed forces at field sites. It could potentially be used to fill this gap for universal blood group testing and contribute to the reduction of HDFN.

PATIENTS AND METHODS

This will be a cross-sectional blinded study of mothers and their neonates at delivery in the labour ward of Korle-Bu Teaching Hospital. By means of a standardized form, socio-demographic, past and current obstetric details, condition of babies at birth will be documented. For each mother/baby pair, 2 ml each of maternal and cord blood will be tested by standard laboratory methods for ABO-Rh blood group at the blood bank. This will be the gold standard. Additionally, capillary blood from the mother and baby will be tested with the Eldon Card kit by trained doctors and nurses to determine their ABO-Rh blood groups. Results of the Eldon card method will be compared to the gold standard. Ethical approval and informed consent will be obtained.

RESULTS

The Eldon card will be a rapid and easy to handle method of determining the ABO-Rh blood groups of mothers and their newborns at the point of care. The results of the Eldon card method will be comparable to those of the gold standard method.

CONCLUSIONS

The Eldon card will be a suitable alternative method for blood group determination for mothers and their newborns at the point of care. It therefore has the potential to help reduce the morbidity and mortality associated with HDFN by improving access to blood group testing, and thus creating the opportunity for timely management.

Microcirculation and oxygen transport

ABS 37

HEME-OXYGENASE EXPRESSION FOLLOWING PRETERM BIRTH: EVIDENCE OF A FEED-FORWARD MECHANISM DRIVEN BY OXIDATIVE STRESS

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INTRODUCTION

In the preterm neonate, high blood flow through the microvasculature is associated with physiological instability and poor outcome in the first 72 hours of life. Carbon monoxide (CO) has been associated with microvascular dilatation during circulatory transition. CO is produced by heme oxygenase (HO). Two isoforms exist with HO-1 induced in response to oxidative stress and therefore of interest in the preterm neonate. In the presence of oxidative stress, HO-1 can be truncated, allowing for nuclear translocation and action in a feed-forward manner. The aim of the present study was to characterise HO-1 expression in our previously established guinea pig model of the preterm neonate.

PATIENTS AND METHODS

Preterm (GA 62 ± 1) and term (GA 69 ± 1) outbred, tri-colour guinea pigs were delivered by caesarean section (normal gestation in our population is 71 days). Microvascular blood flow was assessed by laser Doppler flowmetry every 2 h from birth. Tissues (skin) were collected from fetuses (at time of caesarean section) and neonates at 10 h and 24 h postnatal age. HO-1 protein levels (full 32 kDa and truncated 28 kDa) were quantified by western blot (StressGen/Assay Designs Antibody [ADI-SPA-894-F]). Markers of oxidative stress (GSH/GSSG ratio, oxidised proteins, lipid peroxidation and total antioxidant capacity) were related to HO expression and microvascular status.

RESULTS

Truncated HO-1 (28 kDa) expression increased after birth in preterms ($p = 0.03$) but not in terms ($p = 0.96$): by 10 h, levels of truncated HO-1 were significantly higher in preterms compared to terms ($p < 0.0001$). No upregulation of full length (32 kDa) HO-1 in preterms ($p = 0.20$) or terms ($p = 0.08$) occurred at this time. By 24 h, levels of 28 kDa HO-1 decreased in preterm females ($p = 0.02$). However, levels remained elevated in preterm males ($p = 0.88$). 32 kDa HO-1 expression increased from 10 h to 24 h in male preterms ($p = 0.002$). This was not observed

in preterm females (p = 0.22) or terms (p = 0.54). There was no correlation between microvascular blood flow and HO-1 expression in terms at 24 h postnatal age (32 kDa: p = 0.20, r = -0.36; 28 kDa: p = 0.42, r = 0.23). In preterms, microvascular blood flow correlated with 32 kDa (p = 0.03, r = 0.60) but not with 28 kDa HO-1 (0.47, r = -0.20).

CONCLUSIONS

HO-1 expression is highest in those with microvascular dysfunction: preterm males. The feed-forward mechanism in males supports our hypothesis of preterm male uncontrolled vasodilatation, driven in part by carbon monoxide, contributing to cardiovascular compromise. We have preliminary evidence that oxidative stress may drive excessive HO-1 expression in preterm (male) neonates and that this pathway represents a potential therapeutic target.

ABS 38

TEMPORAL CHANGES IN MICROVASCULAR FUNCTION FOLLOWING PRETERM BIRTH IN GUINEA PIGS

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INTRODUCTION

Survival into adult life is now the expected norm for most individuals born preterm. While cardiovascular perturbation in the newborn period has been well described, the late cardiovascular morbidity of preterm birth is only now starting to be recognised. The mechanisms underpinning these alteratons in CVS function in both neonatal and later are unclear, but may in part reflect altered microcircuatory function. We have developed a unique guinea pig model of preterm birth with which to track longitudinal changes in microcirculatory function throughout the life course.

PATIENTS AND METHODS

Outbred guinea pigs were delivered at term (~GA d 69) or preterm via induction of labour (GA d 62). Pups underwent laser Doppler assessment of microvascular blood flow at 24 h postnatal age, weekly to weaning (3 weeks corrected postnatal age) and monthly until 8 months of age. Linear mixed regression was used to investigate the association of blood flow with gestational and postnatal age. Blood flow changes over time were analysed via random effects generalised least squares regression with bootstrapping (1,000 repetitions).

RESULTS

Patterns of microvascular blood flow from birth to 1 month postnatal age were significantly different between preterm and term guinea pigs (p = 0.001). In term pups, blood flows peaked at 1 week postnatal age (p = 0.008). Blood flow then returned to birth levels and remained stable from the 2nd week of life (week 2: p = 0.42, week 3: p = 0.66; week 4: p = 0.58). In preterm animals, blood flow peaked at 2 weeks corrected postnatal age (3 weeks chronological age, p < 0.0001) followed by a rapid decrease in flow back to baseline levels.

CONCLUSIONS

Preterm animals have persistent differences in microvascular blood flow compared to term controls. These differences may contribute to the establishment of compromised microvascular regulation and the increased risk of cardiovascular disease in ex-preterm adult populations.

ABS 39

EXPLORING CEREBRAL AUTOREGULATION (AR) IN MODERATE AND SEVERE NEONATAL HYPOXIC-ISCHEMIC ENCEPHALOPATHY (HIE) DURING WHOLE BODY HYPOTHERMIA (WBH)

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INTRODUCTION

Neonatal hypoxic-ischemic encephalopathy (HIE) carries an increased risk of altered cerebral blood flow which may be an important determinant in the on-going structural brain damage. Therapeutic whole body hypothermia (WBH) induces a general hypodynamic circulatory state and decreases cellular metabolic activity. Yet, the impact of this haemodynamic adaptation on autoregulation capacity has not been fully characterised.

AIMS
Systematic approach to cerebral autoregulation (AR) during hypothermia and re-warming in neonates with moderate-severe HIE.
PATIENTS AND METHODS
24 HIE neonates underwent continuous aEEG, cerebral oxymetry (TOI) and invasive blood pressure (MABP) monitoring on day 1 (D1) (12 h), D2 (6 h) and D3 (6 h) of WBH and during rewarming (D4, 12 h). MRI was performed at 7-14 d. The bivariate autoregressive spectral coherence (BiAR-COH) method (Riera et al., J Pediatr) was used to analyse the relationship between spontaneous changes in MABP and TOI (high BiAR-COH indicating impaired AR). The aEEG findings were classified as abnormal if burst suppression , low voltage, inactive trace or status. The MRI findings were considered abnormal in case of lesions grading 2 or 3 according to Rutherford et al. (Lancet Neurol). A composite adverse outcome was defined as death or abnormal aEEG and abnormal MRI. Statistics: mixed model analysis.
RESULTS
Differences in BiAR-COH patterns were only identified during D1: neonates with favourable outcome showed stable BiAR-COH whilst infants with composite adverse outcome showed raising BiAR-COH ($p < 0.06$). Overall, BiAR-COH estimators during WBH were lower than those reported in other populations of high-risk infants.
CONCLUSIONS
Haemodynamic changes occurring in early phases of WBH are particularly critical in the most severely injured infants. Careful cardiovascular monitoring and eventual intervention strategies should focus on this time frame.

Organ blood flow and autoregulation

ABS 40

PACAP CAN INFLUENCE THE VASCULAR CHANGES IN THE ANIMAL MODEL OF RETINOPATHY OF PREMATURITY

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INTRODUCTION
The oxygen-induced retinopathy (OIR) is a well-established model of retinopathy of prematurity (ROP). Rat model mimics the human disease, because the retinas of newborn rat pups are similar to that of a 26-week old premature infant and OIR develops on the peripheral area like in humans.
Pituitary adenylate cyclase-activating polypeptide (PACAP) is known to have neuroprotective effects. Several studies have revealed the presence of PACAP and its receptors in the retina. Recent studies reported the protective effects of local PACAP treatment after ischemic and diabetic retinopathy.
In this study we investigated whether PACAP treatment can influence the vascular changes in the rat OIR model.
PATIENTS AND METHODS
OIR was generated by placing the animals in daily alternating 10%/50% oxygen concentrations from postnatal day 0 (P0) to P14, then returned them to room air. Meanwhile, a group of animals received intraperitoneal PACAP treatment from P1-P8. Another group was treated with intravitreal PACAP injection on P11, P14, and P17. Control animals received saline injections in the same ways. On P18-19 retinas were isolated and the vessels were visualized by isolectin staining. The percentages of avascular to whole retinal areas as well as the number of branching points were measured. Electroretinographic (ERG) examination was executed and change in cytokine expression was also determined.
RESULTS
Intravitreal treatment with PACAP remarkably reduced the extent of avascular area (13.25 ± 1.47) compared to that of the non-treated OIR group (20.45 ± 1.51) and saline-treated group (20.40 ± 2.58). Intraperitoneal PACAP treatment did not reveal any differences (18.08 ± 1.82) compared to the control OIR retinas. Retinal images of controls kept in room air did not show vascular alterations. No changes in the number of vessel branching were observed after treatments. Results of ERG examination and alterations in cytokine profile after local PACAP injection further enhanced the protective role of the peptide.
CONCLUSIONS
This is the first study to examine the effects of PACAP in ROP. Although the exact mechanism

is still not known the present results show that PACAP treatment can ameliorate the vascular changes in the animal model of ROP.

ABS 41

DOPAMINE INFUSION IMPROVES CEREBRAL AUTOREGUALTION IN NEWBORN PIGLETS

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INTRODUCTION

Hypotensive neonates who have been treated with dopamine have poorer neurodevelopmental outcome than those who have not been treated with dopamine. We speculate that dopamine therapy might stimulate adrenergic receptors on cerebral arteries and thereby inhibit vasodilation and limit autoregulation at low levels of blood pressures. We tested our hypothesis in a piglet model.

PATIENTS AND METHODS

Cerebral autoregulation (CA) capacity was estimated at different mean arterial blood pressure (MAP) levels in 18 piglets with and without dopamine infusion. Piglets were randomised to start with or without dopamine and to infusion rates of 10, 25 or 40 µg/kg/min. Stable levels of hypotension were induced by gradually inflating a balloon catheter placed in vena cava. At each MAP level small fluctuations in MAP were induced by repeated inflating a balloon catheter in aorta for 30 sec. Cerebral perfusion was monitored by laser doppler flowmetry through a craniotomy. The ratio between the % change of estimated cerebrovascular resistance and the % change of MAP was used to estimate CA capacity. Non-linear regression analysis was used to describe the relation between CA capacity and MAP.

RESULTS

Eighteen piglets aging 4-66 hrs were examined. During measurements $PaCO_2$ (4-6 kPa) and arterial saturation (> 95%) were stable. MAP ranged between 14 and 82 mmHg. Overall, CA capacity improved with increasing MAP until a breakpoint. After that breakpoint the CA capacity was stationary (**Fig. 1**). The breakpoint was 40.5 mmHg (95% range 36.8-42.6) for the piglets when they did not receive dopamine. Below the breakpoint CA capacity increased with the rate of dopamine infusion (+0.7%/[µg/kg/min], 95% CI 0.3-1.1, $p < 0.01$).

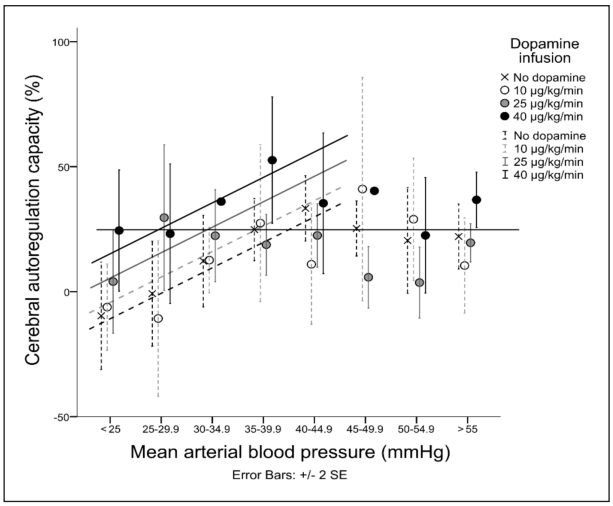

Figure 1 (ABS 41). Cerebral autoregulation capacity and mean arterial blood pressure.

CONCLUSIONS

Surprisingly, dopamine infusion improved rather than impaired the CA capacity in 'hypovolemic', hypotensive newborn piglets.

We speculate that this unexpected finding might be caused by the fact that dopamine reduces the endogenous sympathetic response to comparable low levels of cardiac output. Compared to high endogenous sympathetic tone dopamine might be more 'brain-protective' as dopamine only has minor effect on cerebral arteries.

ABS 42

OPTIMAL MEAN ARTERIAL BLOOD PRESSURE IN PRETERM INFANTS WITH LESS THAN 24 HOURS OF AGE

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INTRODUCTION

Fluctuations in mean arterial blood pressure (MABP) and cerebral blood flow have been

associated with the pathophysiology of brain injury in preterm infants. Using near-infrared spectroscopy, a non-invasive technique to assess cerebral haemodynamics, it is possible to define levels of MABP where cerebral vascular reactivity is strongest ($MABP_{opt}$). We have demonstrated that infants with higher deviations from $MABP_{opt}$ had worse outcome. Our aim is to confirm these findings in preterm infants, using longer monitoring period and changing the protocol from intermittent to continuous brain and systemic monitoring within first 24 hours of life.

PATIENTS AND METHODS

A total of 46 preterm infants born at median gestational age 26^{+4} weeks (23^{+3} to 31) with indwelling arterial catheter were studied for a median of 17 hours. Tissue Oxygenation Heart Rate Reactivity Index (TOHRx), which estimates cerebrovascular reactivity, was calculated as the moving correlation coefficient between slow waves of tissue oxygenation index, measured with NIRS and HR. $MABP_{opt}$ was defined by dividing MABP into 2 mmHg bins and averaging the tissue oxygenation HR reactivity index within those bins. A measurement of divergence from $MABP_{opt}$ was calculated as the absolute difference between mean MABP and mean $MABP_{opt}$.

RESULTS

Results are presented in **Fig. 1**. TOHRx demonstrated a significant correlation with CRIB II ($R= 0.36$, $p < 0.013$). Individual $MABP_{opt}$ was defined in all studied patients, 20% more than in our previous study. Divergence of MABP above $MABP_{opt}$ ($MABP_{above}$) was positively related to intraventricular hemorrhage grade in 17 newborns ($R = 0.55$; $p = 0.033$) in whom haemorrhage was confirmed. Divergence of MABP below optimal value ($MABP_{below}$) was associated with mortality ($R = 0.437$; $p = 0.0027$).

CONCLUSIONS

It has been demonstrated that HR has influence on cerebral haemodynamics in preterm infants. Defining $MABP_{opt}$ based on a index of cerebrovascular reactivity is feasible, safe and non-invasive. This study confirmed that deviations from $MABP_{opt}$ are significantly associated with bad outcome. Moreover, these associations can be seen by monitoring just the first 24 hours of age.

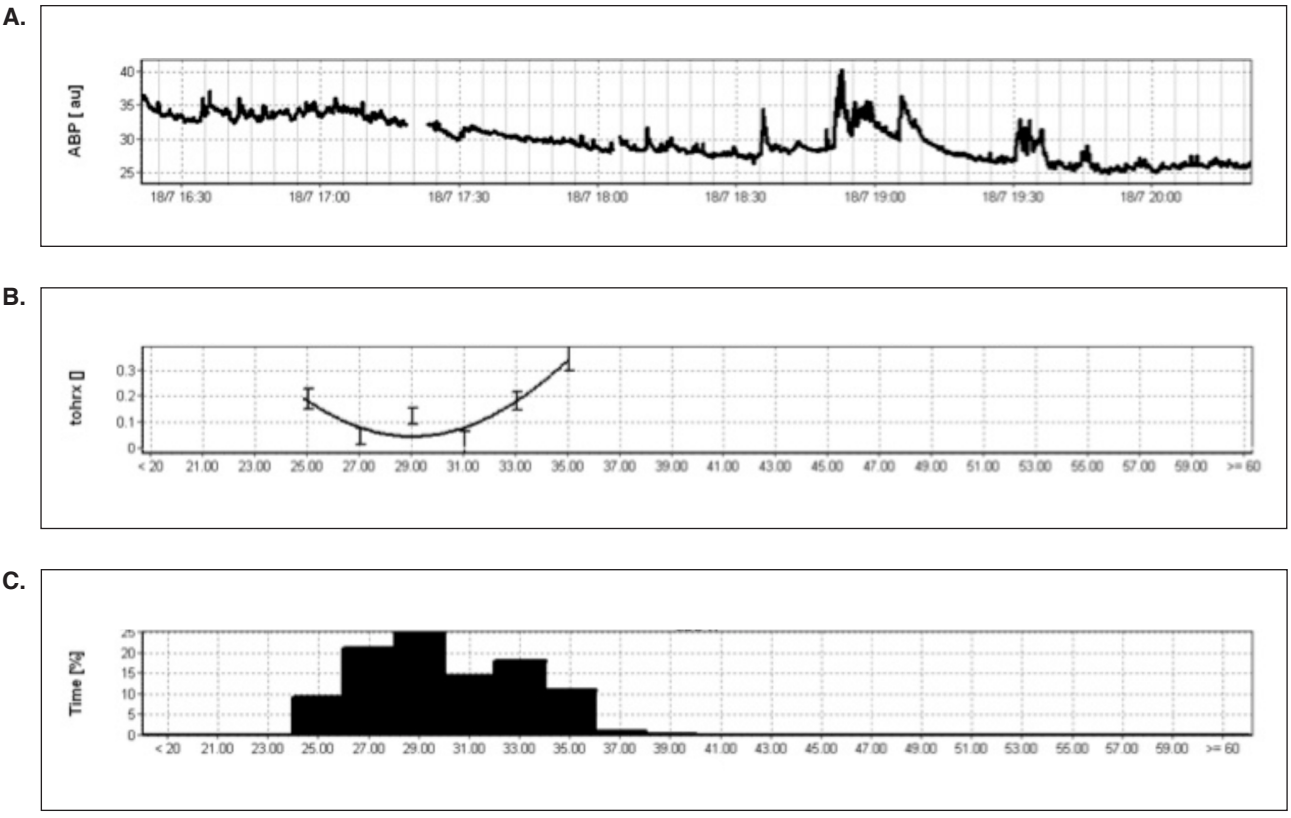

Figure 1 (ABS 42). Arterial blood pressure (ABP) (**A**), tissue oxygenation hearth rate reactivity index (TOHRx) (**B**), and time (**C**).

Pulmonary Hypertension

ABS 43

THE IMPACT OF PREMATURE LUNG DISEASE ON THE MATURATION OF CARDIAC PERFORMANCE IN THE FIRST YEAR OF LIFE: DISCERNING EARLY PREDICTIVE MARKERS OF CHRONIC LUNG DISEASE

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INTRODUCTION

Premature infants with lung disease may exhibit altered myocardial structural programming resulting in decreased ventricular function. Two-dimensional speckle tracking echocardiography (2DSTE) derived strain imaging provides a reliable assessment of global cardiac function in premature infants. The primary aim of this study was to discern the impact of premature lung disease on cardiac adaptation in the first year of life with 2DSTE derived strain. The secondary aim was to determine if strain imaging could predict the development and severity of chronic lung disease in premature infants.

PATIENTS AND METHODS

115 premature infants (26 ± 2 weeks) were prospectively enrolled and longitudinally followed over the 1st year of life through the Premature and Respiratory Outcomes Program (NCT01435187). Ventricular systolic changes in cardiac function were assessed using myocardial strain. A lower magnitude of strain value indicates decreased function. Measurements of right (RV) and left ventricular (LV) strain were derived by 2DSTE and compared at five time points; day of age one and three (n = 30), 32 weeks and 36 weeks post-menstrual age (PMA) (n = 115), and at one year corrected age (n = 80). The primary outcome was bronchopulmonary dysplasia (BPD), as defined by the NHLBI severity-based Workshop definition (no/mild vs. moderate/severe) and the Physiological definition (yes vs. no BPD).

RESULTS

RV strain increases over the first year of life (p = 0.004), while LV strain remains relatively unchanged from birth to one year of life (p = 0.34) (**Fig. 1**). Sixty-five infants developed moderate/severe BPD according the NHLBI Workshop definition and 66 infants were classified as having BPD according to the Physiological definition. At 32 weeks, 36 weeks and one year corrected age, RV strain was significantly lower in the infants with moderate/severe BPD, while there was no difference in LV strain stratified by lung disease (**Fig. 1**). The same maturational patterns of RV and LV strain were evident for the Yes and No BPD groups, according to the Physiological definition.

CONCLUSIONS

RV strain increases with maturation, reflecting physiological changes in postnatal loading conditions. LV strain remains preserved, regardless of BPD severity, suggesting relative constant LV function with maturation. Infants who develop BPD have decreased RV strain as early as 32 weeks PMA that persists to one year corrected age. The RV manifests a pre-clinical arrest of function lending itself as a potential early marker of BPD development in premature infants.

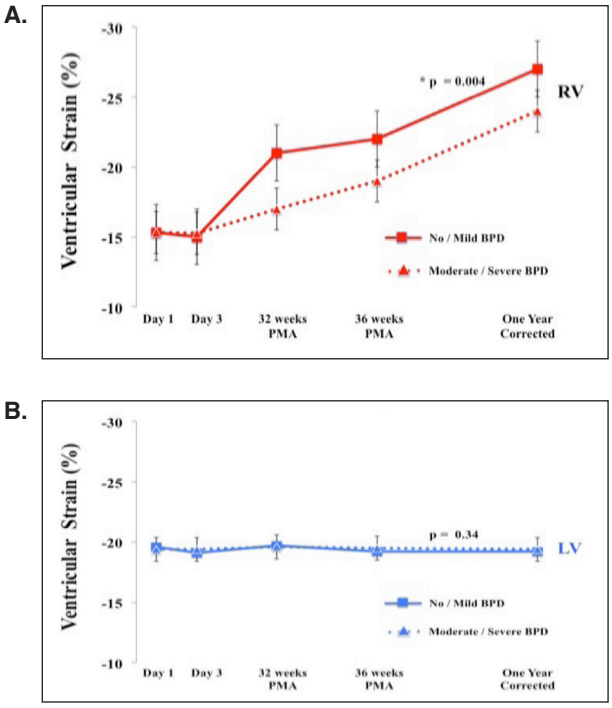

Figure 1 (ABS 43). Right (**A**) and left (**B**) ventricle strain patterns in the first year of life in premature infants.

ABS 44

THE MYOCARDIAL ARCHITECTURE CHANGES DUE TO PERSISTENT PULMONARY HYPERTENSION OF THE NEWBORN IN AN OVINE ANIMAL MODEL

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INTRODUCTION

Despite recent improvements of therapeutic modalities persistent pulmonary hypertension of the newborn remains a syndrome with high morbidity and mortality. The histological changes in the lungs are well described, but the effects on the heart are relatively poorly understood, albeit that congestive heart failure is relatively common. Knowledge of any changes in myocardial architecture especially in the setting of heart failure in persistent pulmonary hypertension is lacking, and could aid in the explanation of the prevailing high mortality. We studied the changes in ventricular mural architecture in an ovine model of persistent pulmonary hypertension using diffusion tensor imaging.

PATIENTS AND METHODS

Persistent pulmonary hypertension was induced by antenatal ligation of the arterial duct in 6 ovine fetuses. The hearts were compared *ex-vivo* with 5 matched control hearts, using diffusion tensor magnetic resonance imaging. This technique measures the spontaneous diffusion of water as a surrogate measure of the orientation of the cardiomyocytes. An overall anatomical evaluation along with a quantitative and qualitative assessment of the angulations and course of the cardiomyocytes was conducted. Moreover, the orientation of aggregated units of cardiomyocytes, often referred to as sheets, was measured. Further, the hearts were subjected to histological examination including collagen quantification using photographic quantification.

RESULTS

A median increase of 5.1° in angulation of aggregated units of cardiomyocytes, was found in pulmonary hypertension. The increase was largest in the left ventricle (6.5°), but also significant in the right (3.3°). Myocardial volume was significantly increased, at 26.8 ml in the hypertensive animals versus 16.9 ml in controls ($p < 0.001$). However, only discrete thickening of the interventricular septum was found, but no other changes in overall cardiac dimensions were detected. No changes were found in terms of main orientation of cardiomyocytes. In the right ventricle the collagen content was found to be 3.8% in hypertensive hearts compared with the 1.6% in controls, $p = 0.048$. In addition, we observed a previously undescribed subepicardial layer of strictly longitudinally oriented cardiomyocytes confined to the right ventricle in both hypertensive and control hearts.

CONCLUSIONS

The changed angulations of aggregated units within the maintained normal gross anatomy indicate an impeded capability for myocardial rearrangement and repacking. Both left and right ventricular myocardial remodeling along with myocardial fibrosis seem to play a part in the etiology of persistent pulmonary hypertension. In addition we uncovered a hitherto unreported new anatomical arrangement of right ventricular mural architecture.

Transfusion and volume therapy

ABS 45

EFFECT OF WITHHOLDING FEEDS ON TRANSFUSION-RELATED ACUTE GUT INJURY IN PRETERM INFANTS – A RANDOMISED CONTROLLED TRIAL

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INTRODUCTION

Recent retrospective observational studies about Necrotising Enterocolitis (NEC) arising within 48 hours of transfusion revealed its incidence as 20-25% and most of these were surgical NEC. Definition of Transfusion-Related Acute Gut Injury (TRAGI), which may end up with NEC, is first proposed in 2011 with several different possible mechanisms.

The aim of this study was to examine the possible effect of withholding feeds during red blood cell transfusion on the incidence of TRAGI.

PATIENTS AND METHODS

The study was conducted between December 2013 and January 2015 in our NICU. Inclusion criteria were: < 32 weeks of gestational age and 7 days old infants, receiving full enteral feeding and red blood cell transfusion. Infants with complex cardiac anomalies, severe sepsis, dysmorphic features and history of asphyxia were excluded. Transfusion decision was made by the attending physician and all the transfusions lasted 3 hours. Control group went on feeding without any change in the regimen while intervention group did not receive enteral feeding for about 8-12 hours during the peritransfusion period. Primary outcomes were feeding intolerance and/or NEC (stage ≥ 2) during the first 72 hours after transfusion. Modified Bell's criteria were used for the diagnosis of NEC.

RESULTS

Feedings were withheld 74 times (intervention group) and continued for 80 times (control group). Gestational ages and birth weights of the babies were 27.5 ± 2.5 vs. 27.2 ± 2.5 and 992 ± 294 vs. 934 ± 259 g respectively. Demographic characteristics were similar between groups. Only 2 babies in the control group were diagnosed as NEC but this was statistically non-significant ($p = 0.498$). Besides, there was no difference in the incidence of feeding intolerance during the first 72 hours of transfusion ($p = 0.369$).

CONCLUSIONS

According to our knowledge, this is the first prospective randomized study in the literature. No statistically significant difference observed in the incidence of feeding intolerance and NEC with withholding feeds during transfusion. The hypothesis that transfusion causing mesenteric perfusion abnormalities and ending up with gut injury due to reaction with concurrent ongoing feeding was not supported by our results.