September 21st, 2023 8:30 - 10:30

PLENARY SESSION 4 - YOUNG INVESTIGATOR PRIZE SESSION

ID 6. Preterm infants on early solid foods and neurodevelopmental outcome – a secondary outcome analysis of a randomized controlled trial

Doctor Margarita Thanhaeuser[1], Doctor Fabian Eibensteiner[1], Doctor Margit Kornsteiner–Krenn[1], MSc Melanie Gsoellpointner[2], Doctor Sophia Brandstetter[1], Doctor Renate Fuiko[1], Doctor Mercedes Huber–Dangl[1], Doctor Christoph Binder[1], Prof. Alexandra Thajer[1], Prof. Bernd Jilma[2], Prof. Angelika Berger[1], Prof. Nadja Haiden[3]
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Background: Introduction of solid foods in preterm infants is a highly discussed topic and evidence–based recommendations do not exist so far. Aim of this study was to examine whether two different timepoints of introduction of solid foods in preterm infants have an impact on neurodevelopmental outcome in the first three years of life.

Methods: This is a secondary outcome analysis of a prospective, randomized, two arm intervention trial of very low birth weight infants randomized to an early (10–12th week corrected age) or a late (16–18th week corrected age) complementary feeding group. Neurodevelopmental outcome was assessed at one and two years corrected age, and at three years, four months uncorrected age using the Bayley Scales of Infant–Toddler Development, third edition, German norms.

Results: In total, 177 infants were randomized, 89 to the early group and 88 infants to the late group with a median gestational age of 27+1 weeks in both groups. 91%, 89%, and 71% of infants were available for analysis at the three timepoints. To evaluate differences in neurodevelopmental outcome between study groups, a linear mixed effects model was fit through study group, gestational age at birth, sex, nutrition at discharge, highest education of parents, and IVH with a random intercept to adjust for possible correlation between siblings of multiple births. No significant differences in neurodevelopmental outcome between groups were found.

Conclusion: The timepoint of introduction of solid foods had no impact on neurodevelopmental outcome at one and two years corrected age, and at three years, four months uncorrected age.

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Bayley–III assessment at one and two years corrected age, and at three years, four months corrected age presented as median (IQR). P–values (linear mixed effects model) <.05 = statistically significant.

Bayley–III assessment at one and two years corrected age, and at three years, four months corrected age presented as median (IQR). P–values (linear mixed effects model) <.05 = statistically significant.

None declared

ID 92. REDUCED LUNG FUNCTION DURING CHILDHOOD AFTER FETAL GROWTH RESTRICTION IN DISCORDANT IDENTICAL TWINS

Miss Jip A. Spekman[1], Mr Joël Israëls[1], Mrs Ilja de Vreede[1], Mrs Mady Los[1], dr J J Miranda Geelhoed[1], Prof dr Monique C Haak[1], dr Arno A W Roest[1], dr Jeanine M M van Klink[1], Prof dr Enrico Lopriore[1], dr Sophie G Groene[1]

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Background: Fetal malnutrition can negatively affect lung development, leading to increased respiratory morbidity and reduced lung function later in life. Yet, studies regarding the impact of fetal growth restriction (FGR) on lung function in singletons are subject to genetic, obstetric, and maternal factors potentially influencing the outcomes. Therefore, we aim to investigate childhood lung function in monochorionic (MC) twins with selective FGR (sFGR) eliminating these confounding factors.

Methods: Spirometry was performed in MC twins with sFGR born in our center between 2002–2017. sFGR was defined as birth weight discordance ⩾20%. Outcome measures consisted of forced expiratory volume in one second (FEV1), forced vital capacity (FVC), residual volume (RV), total lung capacity (TLC), and transfer factor for carbon monoxide (TLCO). All outcomes were compared between the smaller and larger twin.

Results: We included 39 twin pairs with sFGR who performed spirometry of sufficient quality. The median gestational age at birth was 34.3 (interquartile range (IQR) 32.1–36.0) weeks with median birth weights of 1500 (IQR 1160–1880) grams for the smaller twin and 2178 (IQR 1675–2720) grams for the larger twin. The median age at spirometry was 11 (IQR 10–14) years, with median study heights of 149.4 (IQR 138.0–

164.3) cm and 153.3 (IQR 141.1–167.2) cm for the smaller and larger twin, respectively. Smaller twins had significantly lower z–scores for FEV1 (–0.99 vs. –0.55, p=0.001), FVC (–0.61 vs. –0.09, p<0.0001) and TLCO (–0.47 vs. 0.18, p<0.0001) compared to larger twins. We found no difference in FEV1%FVC, RV, TLC and RV%TLC.

Conclusion: Although being genetically identical, sFGR in MC twins is associated with a reduction in static lung volume with an equivalent decrease in dynamic lung function, suggesting that adverse growth conditions in utero negatively affect lung development and function. This can contribute to an increase in respiratory morbidities later in life.

None declared

ID 413. MYOCARDIAL STRAIN IN NEWBORN PIGLETS EXPOSED TO HYPOXIA-ISCHEMIA RANDOMIZED TO REMOTE ISCHEMIC POSTCONDITIONING AND THERAPEUTIC HYPOTHERMIA OR HYPOTHERMIA ALONE

Miss Sofie Schaaning[1], Lærke H. Hansen[1], Ted C.K. Andelius[1], Hannah B. Andersen[1], Mette V. Pedersen[1], Regitze Pinnerup[1], Tine B. Henriksen[1], Kasper J. Kyng[1]

[1]Aarhus University Hospital / Department of Paediatrics, Aarhus, Denmark

Background

Hypoxia–ischemia (HI) at birth compromises all organs of the newborn including the cardiovascular system. Remote ischemic postconditioning (RIPC) is a potential neuroprotective treatment following HI. The effect of RIPC may in part be attributed to effects on cardiac function. In newborn piglets subjected to global HI and randomized to either RIPC and therapeutic hypothermia (TH) or TH alone, we examined serial measures of left ventricle longitudinal (LS) and circumferential strain (CS).

Methods

Twenty–six newborn anaesthetized piglets were exposed to a standardized 45 minutes global HI insult, and randomized to treatment with RIPC+TH (n=13) or TH alone (n=13). RIPC was performed as four cycles of occluded blood flow in both hind limbs for five minutes, followed by five minutes reperfusion, repeated at 1, 12, and 24 hours after the insult. Echocardiography was conducted before the insult, during the last 15 minutes of hypoxia, and 1, 6, 24, and 44 hours after the insult. Left ventricle myocardial strain was measured, blinded to treatment group, using 2D speckle tracking. LS was measured from apical four chamber view and CS at the papillary muscle level from short axis views.

Results

Left ventricular LS and CS values of piglets exposed to RIPC+TH or TH alone were comparable between groups at all measured time intervals (Figure 1 A–B). In both groups, LS and CS decreased during hypoxia, then increased until 24 hours after the insult, followed by a decline to below baseline levels at 44 hours after HI.

Conclusions

Newborn piglets subjected to RIPC+TH versus TH alone after a standardized global HI insult had similar left ventricle LS and CS during 44 hours after the insult, suggesting that RIPC did not alter myocardial strain after HI.

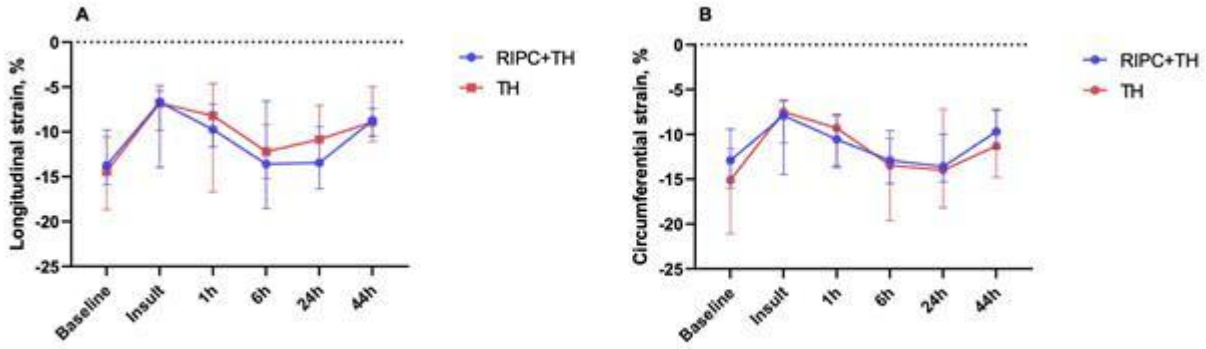

Figure 1. Changes in (A) longitudinal strain, (B) circumferential strain before, during, and after HI. Each point represents median with interquartile range.

None declared

ID 501. DEVELOPMENT OF A HUMAN SERUM ALBUMIN PREDICTION MODEL USING A LARGE REAL-WORLD DATASET OF TERM AND PRETERM NEONATES

Doctor Zoë Vander Elst[1,2], Annouschka Laenen[3], Jana Deberdt[4], Lotte Delemarre[4], Professor Doctor Pieter Vermeersch[5], Professor Doctor Gunnar Naulaers[1,2], Professor Doctor Karel Allegaert[1,6,7], Professor Doctor Anne Smits[1,2]

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Background

Human serum albumin (HSA) is the most abundant plasma protein. Plasma levels of HSA are influenced by different factors and may alter the distribution of HSA–bound drugs. To understand drug exposure (pharmacokinetics, PK) and drug effects (pharmacodynamics, PD) in neonates, knowledge on physiology in early life is needed. This study aims to describe longitudinal trends in real–world HSA plasma levels in a large neonatal cohort, to explore the impact of maturational and non–maturational covariates on HSA plasma levels, and to develop a prediction model for HSA plasma levels in neonates.

Methods

Data from neonates admitted to the NICU of University Hospitals Leuven between June 2015 and April 2017, with postnatal age (PNA) of 28 days or less, were

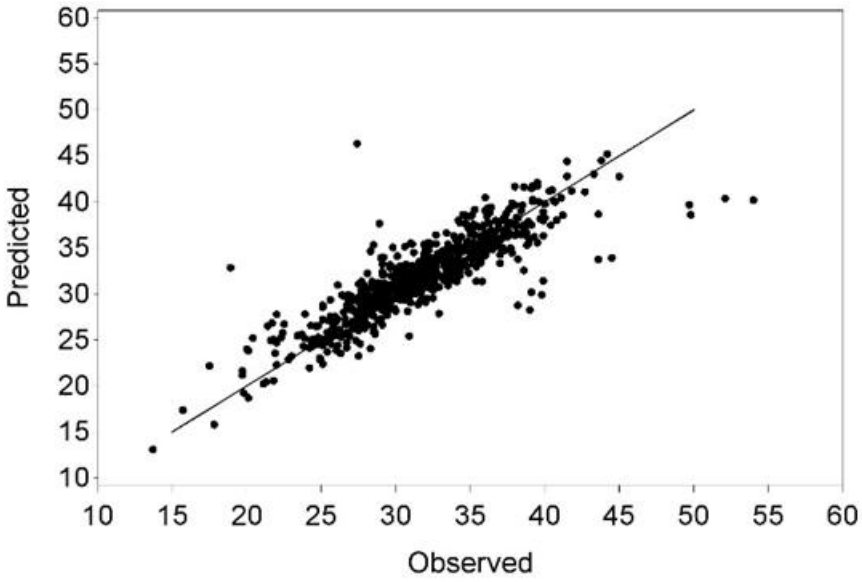
retrospectively collected from patient files. To define covariate effects on HSA plasma levels over time, linear mixed models were used for modelling random effects to account for the repeated measures structure of the data. Univariable analyses were performed and a multivariable prediction model was developed, using a backward model selection procedure with a 1% significance level for elimination of terms.

Results

A total of 848 neonates were included with median (IQR) gestational age (GA) of 35 (32–38) weeks and birth weight (BW) of 2400 (1640–3130) grams. Longitudinal analyses showed an increase in HSA with PNA and GA. Univariable analyses revealed a significant association of PNA, GA, BW, current weight, sepsis, ibuprofen use, respiratory support, ventilation, C–reactive protein, total and direct bilirubin, and total plasma protein with HSA plasma levels (P–value <0.05). Taking interaction with time into account, a complex HSA prediction model was developed with high model performance (R^2 = 77.5%). Next, a clinically applicable, more simplified HSA prediction model was developed containing 10 statistically significant covariates (model performance R^2 = 76.2%).

Conclusion

The developed HSA prediction models, based on a large cohort of term and preterm neonates, integrate multiple (non–)maturational covariates providing an accurate prediction of HSA plasma levels in neonates. Together with drug albumin–binding data, these can be used in neonatal PK/PD analyses to improve modelling and unbound drug exposure prediction and, consequently, drug dosage in neonates.



Method	Rho (95% CI)	R-squared
Simplified model		
All data points	0.867 (0.846; 0.884)	0.751
Weighted average over days	0.872 (0.849; 0.895)	0.762

Scatterplot, with predicted and observed HSA plasma levels (g/dL), and model performance of the simplified HSA prediction model.
(Rho = Pearson correlation)

Scatterplot, with predicted and observed HSA plasma levels (g/dL), and model performance of the simplified HSA prediction model.
(Rho = Pearson correlation)

None declared

ID 520. Stress exposure during NICU admission: the challenges faced by preterm infants

Mrs Naomi Meesters[1], Dr. Gerbrich van den Bosch[1], dr. Joost van Rosmalen[2,13], dr. Maria Luisa Tataranno[3], Dr. Lotte Haverman[4], Dr. Willem de Boode[5], Dr. Peter Dijk[6], Dr. Frank Schuerman[7], dr. Marlou Raets[8], dr. Christ–jan van Ganzewinkel[9], Prof. dr. Enrico Lopriore[10], Prof. Dr. Anton van Kaam[11], Prof. Dr. Irwin Reiss[1], Prof. Dr. Manon Benders[3], Prof. Dr. Monique van Dijk[1,12], Dr. Sinno Simons[1]

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Background

NICU admission is known as a potentially very stressful period in the preterm infants' life with an important impact on the short and long-term development of the child. This study aims to describe stress exposure for preterm infants born with a gestational age below 29 weeks during the first 28 days of NICU admission.

Methods

This is a national multicenter observational cohort study with a one-year inclusion period in all 9 Dutch NICUs. All premature infants born in the Netherlands with a gestational age below 29 weeks were eligible for inclusion. Data collection included patient characteristics and the previously developed NeO-stress score, consisting of 38 items including their severity index. The stress score were calculated per day for all infants and a cumulative score during the first 28 days was determined for the infants that were admitted this complete period.

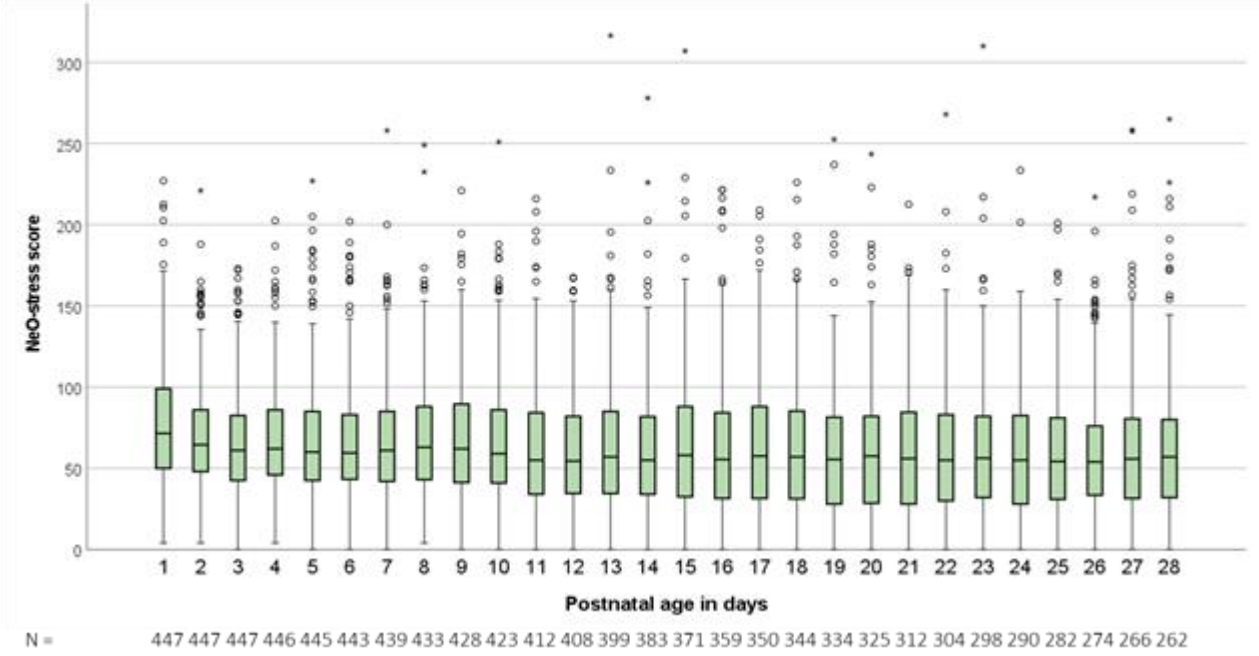
Results

A total of 447 patients, 74% of all eligible patients, were included in this study. These 262 boys (59%) and 185 girls (41%) had a median gestational age of 27 weeks and 2 days (IQR 26+1 to 28+2 weeks) and a birthweight between 450 and 1635 grams. NeO-stress scores per day ranged from 0 to 317 with a median score of 59.5 (IQR 37.5 to 84.5). Median stress exposure per day was highest on the day of admission (71.5, IQR 50 to 99) and showed an overall decrease during the first 28 days ($r = -0.12$, $p<0.001$), see figure 1. The cumulative stress score during the first 28 days ($N = 262$), was negatively correlated with gestational age ($r = -0.50$, $p<0.001$).

Conclusion

Our preliminary results show that there is an overall very high, but variable, daily stress exposure in preterm infants during NICU admission with an overall decrease

over time during the first 28 days. Gestational age is negatively associated with the cumulative exposure to stress. A better understanding of other factors associated with the level of stress is important in order to determine ways to decrease this stress and its negative consequences. These factors will be analyzed and available to present at the congress.



Stress exposure during the first 28 days of life in preterm infants with a gestational age less than 29 weeks

Stress exposure during the first 28 days of life in preterm infants with a gestational age less than 29 weeks

None declared

ID 677.TRENDS IN MORTALITY AND NEUROLOGICAL INJURIES IN VERY PRETERM OUTBORN AND INBORN SURVIVORS CARED FOR IN AUSTRALIAN AND NEW ZEALAND NEONATAL INTENSIVE CARE UNITS: 1995 TO 2019

Doctor Giannina Tinoco Mendoza[1,2], Doctor Sadia Hossain[2,3], Associate Professor Amy Keir[4], Associate Professor Michael Stewart[5], Associate Professor Kathryn Browning Carmo[6], Doctor Lucy Cooke[7], Doctor Jonathan Davies[8], Doctor Joanne Hegarty[9], Doctor Ruth Sinclair[10], Doctor Malcolm Battin[9], Associate Professor Tim Schindler[1,2], Doctor Srinivas Bolisetty[1,2], Professor Kei Lui[1,2]

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Background: Very preterm infants (VPT), born outside (outborn) tertiary centres with on-site neonatal intensive care units (NICUs), are known to have higher rates of mortality and neurodevelopmental impairment than those inborn. This group sought to examine whether contemporary clinical practice and established coordinated regional retrieval services, has improved the outcomes for high-risk outborn infants over the preceding 25 years (1995 – 2019).

Methods: A retrospective cohort study of the ANZNN NICU population database, for infants born at 22–31weeks gestational age (GA) and admitted to ANZ tertiary NICUs. Outborn and inborn infants were compared for trends in mortality at discharge and survival with serious neurological injury (SNI; presence of intraventricular haemorrhage grade 3/4 or periventricular leukomalacia) for infants born at 22–25 weeks, 26–27 weeks and 28–31 weeks GA, across five epochs (1995–1999, 2000–2004, 2005–2009, 2010–2014, and 2015–2019).

Results: 9370 (12%) of 78,517 VPT infants, were outborn. The outborn mortality was higher than for inborns (10% vs 7%, p<0.001); the VPT mortality rate gap narrowed over time from Epoch 1 to Epoch 5 (Epoch–1: 14.1% outborn v 9.8% inborn, p<0.001; Epoch–5: 7.4% v 5.9% respectively, p<0.01). While inborn mortality improved, the Difference–in–difference (DID) analysis showed overall outborn mortality improvement surpass that of inborns (estimate 2.8%, SE 1.0%, p=0.005). Reduction of mortality and SNI rate among survivors of the three gestational age groups varied for both outborn and inborn infants (Figure 1). Improvements, including fewer SNI outborn survivors, were seen in the higher gestation subgroups. Least favourable outcomes were seen in 22–25 weeks GA outborn infants, having highest mortality rate compared to their inborn counterparts, as well as an increase in SNI survivors.

Conclusion: Survival to discharge increased and SNI among survivors decreased among VPT NICU infants in Australia and New Zealand from 1995 to 2019. Despite improving performance over and above the inborn gains, outborn VPT infants continue to have higher mortality and SNI among survivors than the inborns. Notwithstanding the evolution of regionalised neonatal retrieval services, it remains critical to support optimal maternal transport of pregnancies especially those born at <26 weeks GA to prevent death and neurodevelopmental disability in survivors.

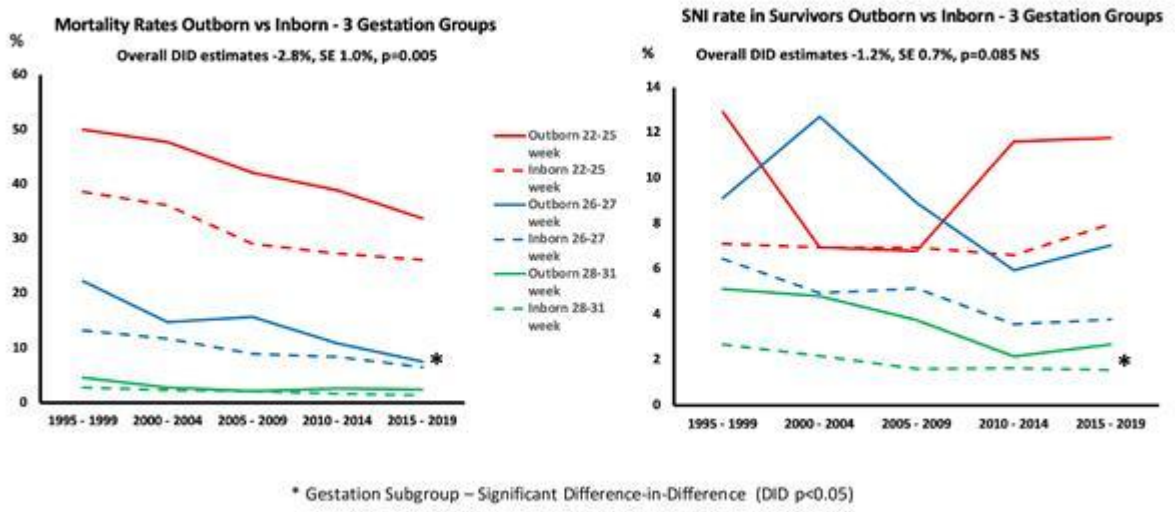

Figure 1. Variations in Mortality and Survivor SNI Rates for VPT Outborn and Inborn Infants cared for in Australian and New Zealand NICUs

1995 — 2019

Figure 1. Variations in Mortality and Survivor SNI Rates for VPT Outborn and Inborn Infants cared for in Australian and New Zealand NICUs

1995 — 2019

None declared

ID 803. A RANDOMISED TRIAL OF ROUTINE OR SELECTIVE APPLICATION OF A FACE MASK FOR BREATHING SUPPORT OF PRETERM INFANTS AT BIRTH

Doctor Caitríona Ni Chathasaigh[1,2], Doctor Emma Dunne[1,2], Doctor Lucy Geraghty[1,2], Doctor Madeleine Murphy[1,2], Doctor Eoin O'Currain[1,2], Doctor Lisa McCarthy[1,2], Prof Colm O'Donnell[1,2]

[1]The National Maternity Hospital, Dublin, Ireland, [2]University College Dublin, , Ireland

Background: Most preterm infants breathe spontaneously at delivery. Despite this, the majority have a face mask applied immediately, usually before their heart rate has been determined. Application of a face mask may inhibit spontaneous breathing.

Objectives: To determine whether selectively applying a face mask to give positive pressure ventilation (PPV) to preterm infants for apnoea or bradycardia only, rather than routinely giving face mask continuous positive airway pressure (CPAP) resulted in fewer infants receiving PPV in the first 5 minutes of life.

Methods: Infants born before 32 weeks' gestation were randomly assigned before birth to 'Routine' or 'Selective' groups, stratified by gestational age (GA) [<28 and 28+0– 31+6 weeks]. 'Routine' infants had a face mask applied to give CPAP as soon as possible after birth. 'Selective' infants were placed supine to breathe spontaneously and were not to receive mask CPAP before 5 minutes of life. Infants in both groups were given mask PPV for apnoea or bradycardia (heart rate <100bpm). All other aspects of DR care were the same. The primary outcome was face mask PPV in the first 5 minutes of life. Secondary outcomes in the DR included use of face mask CPAP, face mask PPV, endotracheal intubation, and chest compressions; and

heart rate and oxygen saturations at 5 minutes. Secondary outcomes in the NICU included endotracheal ventilation and surfactant administration.

Results: We enrolled 200 infants; 102 were randomly assigned to “Routine” [mean (SD) GA 28 (2) weeks and birth weight (BW) 1152 (423) g] and 98 to “Selective” [mean (SD) GA 28 (3) weeks and BW 1118 (440) g]. There was no difference in the proportion of babies who received PPV in the first 5 minutes of life [53/102 (52%) vs 62/98 (63%), P = .106] between the groups. More infants in the Routine group received mask CPAP in the DR, in accordance with the protocol. There were no differences between the groups in other secondary outcomes.

Conclusions: Selective application of a face mask for PPV did not result in fewer preterm infants receiving PPV in the DR.

	Routine *n* =102	Selective *n* = 98	*p* value
Primary outcome: Mask PPV first 5 min *	53 (51)	62 (63)	.106
$23^{+0} - 27^{+6}$	28/43 (65)	33/42 (79)	.168
$28^{+0} - 31^{+6}$	25/59 (42)	29/56 (52)	.312
DR outcomes			
Face mask CPAP *	98 (96)	68 (69)	< .001
Face mask PPV *	53 (52)	63 (64)	.077
Endotracheal intubation *	15 (15)	17 (17)	.611
Chest compressions *	3 (3)	4 (4)	.661
HR at 5 minutes (beats/min) #	144 (28)	142 (27)	.667
Oxygen saturation at 5 minutes #	85 (17)	78 (24)	.120
NICU outcomes			
Endotracheal intubation during admission *	60 (59)	59 (60)	.842

* = (%)
# = median (IQR)
Abbreviations: PPV, positive pressure ventilation; DR, delivery room; CPAP, continuous positive airway pressure; HR, heart rate; IQR, interquartile range

Table 1. Outcomes

Table 1. Outcomes

None declared

ID 937. PERINATAL STROKE LESION VOLUME AND TOPOLOGY ARE RELATED TO COGNITIVE IMPAIRMENT AT EARLY SCHOOL-AGE

Doctor Nienke Wagenaar[1,2], Kirstin Walker[2], Professor Manon Benders[1], Doctor Nomazulu Dlamini[2,3]

[1]Department of Neonatology, University Medical Center Utrecht Brain Center and Wilhelmina Children's Hospital, Utrecht University, Utrecht, Netherlands, [2]Neurosciences & Mental Health, Research Institute, Hospital for Sick Children, Toronto, Canada, [3]Division of Neurology, Department of Paediatrics, Hospital for Sick Children, Toronto, Canada

Background

Perinatal arterial ischemic stroke (PAIS) leads to major developmental disabilities, such as motor and cognitive sequelae, as well as epilepsy, language disorders and behavioral problems. Early MRI offers the ability to accurately predict motor disabilities in later life. However, it is still very challenging to predict the effect of PAIS on other developmental domains. This study aims to create voxel-based lesion-symptom maps to identify specific PAIS features associated with adverse cognitive development at early childhood.

Methods

A total of 94 term-born neonates with PAIS, born between 2000-2016, from the Hospital for Sick Children in Toronto (SickKids), Canada (n=45) and the University Medical Center in Utrecht (UMCU), the Netherlands (n=49) were included who had a neonatal MRI available (performed at a mean age of 4.1±3.0 days after birth). Stroke lesion volumes were semi-automatically segmented and used for univariate voxel-based lesion symptom mapping (VLSM). Cognitive development was assessed at a

mean age of 5.2 (0.8) years by the Wechsler Preschool and Primary Scale of Intelligence (WPPSI), that yielded full scale intelligence quotient (FSIQ), verbal and performance intelligence quotient (VIQ and PIQ) and performance speed index (PSI).

Results

Cognitive impairment, defined as a FSIQ below –1SD, was associated with lesions in the left temporo–parietal lobe including the postcentral gyrus and the superior and middle temporal gyrus. In the UMCU, but not in the SickKids, cohort, impaired performance speed (PSI below –1SD) was associated with lesions in the right parietal lobe, specifically the inferior parietal lobe. Stroke lesion volume was negatively correlated with all cognitive subscores and cut–offs were calculated for stroke volume to predict cognitive impairment, ranging between 4.9% and 6.0% of total intracranial volume.

Conclusion

In this multicenter study, we were able to accurately delineate, in a semi–automatic method, stroke lesions on early MRI in a large cohort of 94 patients with PAIS and found that stroke lesion volume and topology on neonatal MRI are associated with cognitive development at early school–age.

None declared.