Neonatal Society Summer Meeting

25th - 26th June 2015

Winchester

Neonatal Society Summer Meeting

Day 1, Thursday 25th June

11.30 – 12.45 Registration, lunch and exhibits

Session 1

Chair: Dr Topun Austin

12.45 Welcome from meeting organiser, Professor Howard Clark.

12.50 Vennila Ponnusamy, The Royal London Hospital
MicroRNA from dried blood spots: a novel biomarker method in newborns after perinatal asphyxia

13.05 Jane Hassell, University College London
Argon augments therapeutic hypothermia in a piglet model of perinatal asphyxia

13.20 Subhabrata Mitra, University College London
Cerebral mitochondrial oxidative metabolism is closely related to electrographic changes during recurrent neonatal seizures following hypoxic-ischaemic encephalopathy

13.35 Manuel Blesa Cábez, University Of Edinburgh
Anatomic labeling of the neonatal brain by longitudinal registration of an adult atlas through intermediate time points in childhood

13.50 **David Harvey Senior Fellowship**

Prof Nikki Robertson, Professor Of Perinatal Neuroscience, University College London
Effective and safe but cheap and practical: new therapies for neonatal encephalopathy

14.50 Tea break, poster walk (A), and exhibits

Session 2

Chair: Prof Neena Modi, President of the Neonatal society

15.30 Sujith Pereira, Royal London Hospital
Early echocardiography does not predict treatment of patent ductus arteriosus in extremely premature infants

15.45 Matt Cawsey, Birmingham Women's Hospital NHS Foundation Trust
Feasibility of pulse oximetry screening for critical congenital heart defects in homebirths

16.00 Sharon Ocansey, Imperial College London
Cardiovascular function and hypertension in young adults born preterm: an interim analysis

16.15 **Tizard Lecture**

Prof Dino A. Giussani, Professor of Developmental Cardiovascular Physiology & Medicine, University of Cambridge
Fetal origins of cardiovascular disease: new treatment strategies

17.15 Close of day
Social programme: conference dinner and cruise aboard the Princess Caroline

Day 2, Friday 26th June

08.30 – 09.00 Registration

Session 3

Chair: Dr Richard Thwaites, General Secretary of the Neonatal Society

09.00 Sabita Uthaya, Imperial College London
Nutritional Evaluation and Optimisation in Neonates (NEON): a randomised double-blind controlled trial of amino-acid regimen and intravenous lipid composition in preterm

09.15 Mark Johnson, NIHR Southampton Biomedical Research Centre, University Hospital Southampton NHS Foundation Trust
Using normalization process theory to implement and embed improved nutritional practices into the routine care of preterm infants in neonatal intensive care

09.30 Sharifa Scerif, Imperial College London
Infant feeding at 3 months of age in a prospective cohort born in a WHO baby friendly hospital: the relationship with mode of delivery

09.45 Stephanie Chan, University of Southampton
Early nutrition and neurodevelopmental outcomes in preterm infants: a systematic review

10.00 Shalini Ojha, University of Nottingham
Epicardial fat is a nutritionally regulated depot of brown adipose tissue newborn infants and children

10.15 Cheryl Battersby, Imperial College London
A prospective population study of the incidence of severe necrotising enterocolitis in English neonatal units

10.30 – 11.15 Coffee break, poster walk (B) and exhibits

Session 4

Chair – Prof Howard Clark, President-elect of the Neonatal Society

11.15 Sandeep Shetty, King's College London
Crossover study of proportional assist versus assist control ventilation in infants with evolving or established BPD

11.30 Alastair Watson, University of Southampton
Investigating the interaction of SP-A and SP-D with respiratory syncytial virus for development of therapeutic treatment of premature neonates

11.45 William Dawes, Queen Mary University Of London
Neonatal intraventricular haemorrhage downregulates notch and activates proliferation in the subventricular zone

12.00 Jenny Ingram, University of Bristol
Preparing for home: increasing parental knowledge, understanding and confidence in caring for their preterm infant before and after discharge home

12.15 Prize-giving – best oral presentation and best poster by trainees

12.20 Young Investigator Prize Lecture
Dr Sara Hillman, Prenatal Cell & Gene Therapy Group, UCL
Parental influences on fetal growth

13.00 – 14.00 Lunch, poster viewing and exhibits

Session 5

Chair: Dr James Boardman, Meetings Secretary of the Neonatal Society

14.00 Joyce O'Shea, Southern General Hospital, Glasgow
A randomized trial of videolaryngoscopy to teach neonatal intubation

14.15 Kate Costeloe, Queen Mary University of London
Bifidobacterium Breve Bbg-001 (B Breve) to prevent necrotising enterocolitis (NEC), late-onset sepsis (LOS) and death: the PiPS trial

14.30 Keynote Speaker
Dr Helen Mactier, Consultant Neonatologist and Honorary Clinical Associate Professor, University of Glasgow
Substance abuse in pregnancy

15.30 – 16.00 Tea, poster viewing, exhibits and close of meeting

Poster walk A: Thursday 25th June 14.50-15.30
Discussant: Dr Divyen Shah

Paul Cawley, Norfolk and Norwich University Hospital
The thermal safety of neonatal magnetic resonance brain imaging at 3.0 tesla

Therese Ibrahim, Norfolk And Norwich University Hospital
'Feed and wrap' versus routine sedation and use of a vacuum infant immobiliser splint: a review of neonatal brain MRI quality and success in two epochs

M Schreglmann, University Hospital Southampton NHS Foundation Trust
Two-year behavioural and cognitive outcomes of children who underwent therapeutic hypothermia for hypoxic-ischaemic encephalopathy

Nuala Calder, North Bristol NHS Trust
Factors associated with coagulopathy and intracranial bleeding in cooled neonates with hypoxic-ischaemic encephalopathy

Mojgan Ezzati, University College London
Neurotoxicity with dexmedetomidine combined with therapeutic hypothermia in a piglet model of perinatal asphyxia

Poster walk B: Friday 26th June 10.30-11.15
Discussant: Dr Andy Ewer

Jenny Pond, NIHR Southampton Biomedical Research Centre, University Hospital Southampton NHS Foundation Trust
Lost opportunities for nutrition-reasons for missed feeds in a tertiary neonatal unit

Anushma Sharma, Bolton NHS Foundation Trust
Survey of perceptions of withdrawal of intensive care in a neonatal intensive care unit

Mary Pedley, Neonatal Transport Service (NeTS), Portsmouth
Iatrogenic hypocarbia and respiratory alkalosis following neonatal transfer

Nigel Hall, University Hospital Southampton NHS Foundation Trust
Age stratified incidence of gastroschsis

Preethish Shetty, Queen Alexandra Hospital, Portsmouth
Postnatally acquired cmv in extremely premature infants: incidence and clinical manifestations, a single centre 4 year case series

Amy Young, Bradford Royal Infirmary
Co-recruitment in neonatal research; our experience of enrolling mothers and babies in multiple interventional studies

Title (Upper case)

MICRORNA FROM DRIED BLOOD SPOTS; A NOVEL BIOMARKER METHOD IN NEWBORNS AFTER PERINATAL ASPHYXIA

Authors *(Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)*

Ponnusamy V[1,2], Kapellou O[3], Yip E[1], Evanson J[4], Michael-Titus A[5], Yip P[5] & Shah D[1,2]

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Institution(s)

[1]Centre of Paediatrics, Blizard Institute, U.K.; [2]NICU, The Royal London Hospital; [3]NICU, Homerton Hospitals; [4]Imaging Services, The Royal London Hospital; [5]Centre of Neuroscience, Blizard Institute, U.K.

Introduction *(include hypothesis)*

MicroRNAs (miRNAs) are non-coding RNAs involved in regulating gene expression. Their study from dried blood spot (DBS) in newborns and their role as a biomarker for hypoxic-ischemic encephalopathy (HIE) for therapeutic hypothermia (TH) are yet to be explored. Hypotheses:1) Extraction and quantification of candidate miRNAs from DBS correlate with miRNA levels obtained from biofluids including plasma, blood-EDTA and urine. 2) Expression of neuro-specific miRNAs correlate with MRI outcomes in babies after TH.

Methods (*include source of funding and ethical approval if required)*

Ethically approved newborns with HIE were prospectively recruited; Group 1 fulfilled standard criteria and received TH and Group 2, with mild HIE did not. Blood, a DBS and urine were collected; plasma was separated from the blood-EDTA. RNA extraction and quantitative RT-PCR were performed on all samples to extract and quantify three candidate miRNAs (RNU6B, Let7b and miR-21). MRIs were reported independently by 2 reviewers.

Results

Of 30 neonates recruited, 19 received TH. 13/19 were predicted to have a favourable outcome based on MRI of cerebral tissue injury described by Rutherford et al(1).Overall, 80% (24/30) were predicted to have a favourable neurological outcome. MiRNAs were extractable from all samples of both groups. Prolonged storage of DBS (range 2 to 191 days) at room temperature did not affect the expression for all 3 miRNAs in plasma, blood and DBS indicating stability of miRNAs. There was a significant positive correlation between DBS and EDTA-blood for RNU6B (R^2=0.27, p=0.005), let7b (R^2=0.50, p=0.0001) and miR-21 (R^2=0.20, p=0.01). The comparison of miRNA expression using mean Ct values for all three miRNAs analysed demonstrated significantly lower Ct values, meaning higher expression in DBS than in plasma, EDTA-blood and urine in both the predicted unfavourable as well as favourable outcome groups of newborns.

Conclusions

It is feasible to study the expression of miRNA from dried blood spots obtained from newborns. This novel method using a very small drop of blood will be valuable for future research of miRNAs as biomarkers for brain injury and the potential for development of other objective bedside biomarkers of brain injury in the newborn.

References *(include acknowledgement here if appropriate)*

1 Rutherford M, et al. Assessment of brain tissue injury after moderate hypothermia in neonates with hypoxic-ischemic encephalopathy: a nested substudy of a randomised controlled trial. *Lancet Neurol* 2010;9:39-45.

Title (Upper case)

ARGON AUGMENTS THERAPEUTIC HYPOTHERMIA IN A PIGLET MODEL OF PERINATAL ASPHYXIA

Authors *(Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)*

Jane Hassell (1), Bobbi Fleiss (2, 3), Kevin D Broad (1), Igor Fierens (1), Daniel Alonso-Alconada (1), Eridan Rocha-Ferreira (1), Alan Bainbridge (4), David Price (4), Go Kawano (1), Mojgan Ezzati (1), Mariya Hristova (1), Robert D Sanders (5), Xavier Golay (6), Pierre Gressens (2, 3) and Nicola J Robertson (1)

Corresponding author e-mail address: n.robertson@ucl.ac.uk

Institution(s)

1) Institute for Women's Health, UCL, 2) Centre for the Developing Brain, King's College London, 3) INSERM, Paris, France, 4) Medical Physics, University College London Hospital, 5) University of Wisconsin, Madison, USA, 6) Institute of Neurology, UCL.

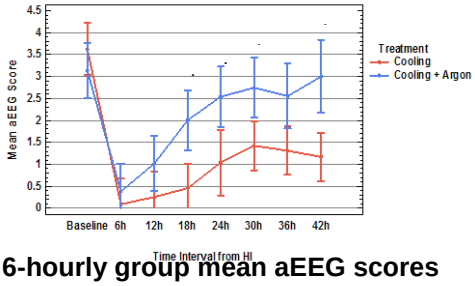
Introduction *(include hypothesis)*

Therapeutic Hypothermia (HT) is standard care for Hypoxic Ischaemic Encephalopathy (HIE), however 50% of treated infants still have adverse outcomes. Phase II clinical trials of Xenon-augmented HT are underway[1], however Xenon is rare, expensive and requires a specialist ventilator. Argon, another noble gas, is safe, 200 times cheaper than Xenon, and provides protection at least equal to Xenon in rodent models[2]. We hypothesised that Argon would augment hypothermic neuroprotection in our piglet model of perinatal asphyxia.

Methods (*include source of funding and ethical approval if required)*

All experiments were performed under UK Home Office Guidelines [Animals (Scientific Procedures) Act, 1986]. This study was funded by a grant from Action Medical Research. Eighteen newborn piglets (<24h) were surgically prepared and intensively monitored. Following quantified transient HI insult piglets were randomised to: (i) HT alone (2-26h, 33.5^{o}C) or (ii) HT + 50% Argon (2-26h). ^{1}H and ^{31}P Magnetic Resonance Spectra were recorded at 2, 24, 48h. Electroencephalogram (EEG) was monitored throughout. Piglets were euthanised after 48h. Brains were fixed and stained for TUNEL (cell death).

Results



6-hourly group mean aEEG scores

Argon was straightforward to deliver through a standard SLE ventilator and was well tolerated. MRS showed significant preservation of whole-brain NTP/ePP and PCr/Pi at 48h after HI in the Argon-HT group compared to HT alone (p=0.01). Protection occurred predominantly in the white matter, with significantly reduced white matter Lac/NAA at 48h (p=0.04). Cell death (TUNEL+ cells) was lower in the Argon-HT group, significant across whole-brain and in caudate and putamen (p<0.02). We observed striking recovery in amplitude-integrated EEG in Argon-HT animals only, with higher mean Hellstrom-Westas scores[3] from 12h onwards compared to HT (p<0.001).

Conclusions

Argon 50%+cooling conferred significant neuroprotection after hypoxia-ischaemia when compared to cooling alone. Both our MRS biomarkers and aEEG recovery speed strongly correlate to neurodevelopmental outcome in babies with HIE[4,5]. Argon may provide a cheaper, more practical alternative therapy to Xenon.

References *(include acknowledgement here if appropriate)*

1. http://www.npeu.ox.ac.uk/toby-xe; **2.** Zhuang et al., Crit Care Med 2012; 40: 1724-30; **3.** Hellstrom-Westas et al., ADC Fetal Neonatal Ed 1995; 72: F34-8; **4.** Toet et al., ADC Fetal Neonatal Ed 1999; 81: 12-23; **5.** Thayyil et al., Pediatrics 2010; 125: e382-95

Title (Upper case)

CEREBRAL MITOCHONDRIAL OXIDATIVE METABOLISM IS CLOSELY RELATED TO ELECTROGRAPHIC CHANGES DURING RECURRENT NEONATAL SEIZURES FOLLOWING HYPOXIC ISCHAEMIC ENCEPHALOPATHY

Authors *(Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)*

Subhabrata Mitra[a], Gemma Bale[b], Sean Mathieson[a], Cristina Uria-Avellanal[a], Judith Meek[a], Ilias Tachtsidis[b] and Nicola J Robertson[a]

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Institution(s)

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[b]Department of Medical Physics and Bioengineering, University College London, UK

Introduction *(include hypothesis)*

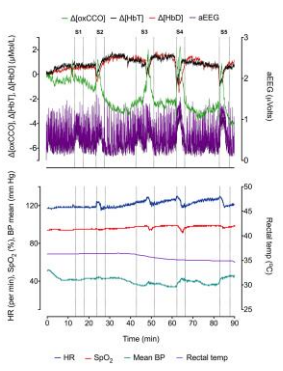
Seizures are common after hypoxia-ischaemia (HI) and induce further neuronal damage beyond the underlying pathology. Cytochrome c oxidase (CCO) plays a central role in mitochondrial oxidative metabolism and ATP synthesis. We hypothesized that broadband NIRS measured changes in oxidation status of CCO (Δ[oxCCO]) would correlate with the changes in the electrical activity during neonatal seizures following HIE.

Methods (*include source of funding and ethical approval if required)*

Ethical approval was obtained (REC reference: 13/LO/0106) and written consent was taken before the study. Recurrent seizures during rewarming (6½ hours after completion of therapeutic hypothermia for 72 hours) in a term infant with severe encephalopathy were studied using a custom-built broadband NIRS system[1], collecting data at 1Hz. Continuous EEG/aEEG data collected over 10 channels and systemic data collected from patient monitor, were synchronized with NIRS data. Mean aEEG was calculated from the mean of the upper and lower values of the aEEG band.

Results

Five electrographic seizures were recorded on the EEG (labelled in the figure as S1 to S5). At the start of each seizure on the aEEG (indicated by a rise in the baseline of the aEEG), the Δ[oxCCO] increased by 3.30 ±1μMol/L. But soon after aEEG activity peaks, the Δ[oxCCO] starts to drop and continues to do so even after the end of each seizure to a progressively lower baseline, which at the end of 90 minutes was -4.19 μMol/L (Figure 1). Δ[HbT] and Δ[HbD] both decreased by 1.51±0.77 μMol/L and 1.50±0.69 μMol/L respectively before the start of each seizure episode, and then returned towards baseline during the seizure. Systemic changes were evident with repetitive seizures. Heart rate and mean arterial blood pressure increased by 5±1.1 beats/min and 5±1.1mm Hg respectively, while peripheral oxygen saturation dropped by 3.2±2.8%during seizures. Rectal temperature fall by 1^0C as



Conclusions

A rapid increase in Δ[oxCCO] at the onset of seizures indicate an increase in mitochondrial energy consumption as the neuronal energy demand increases. Δ[oxCCO] closely correlated with the aEEG changes during seizures. The progressive fall in the Δ[oxCCO] baseline during repeated seizures indicates a continuing depletion of mitochondrial energy state and explain the harmful effects of recurrent seizures.

References *(include acknowledgement here if appropriate)*

1. Bale G, Mitra S, Meek J, Robertson N, Tachtsidis I. Biomedical optics express. 2014;5(10):3450-66.

Title (Upper case)

ANATOMIC LABELING OF THE NEONATAL BRAIN BY LONGITUDINAL REGISTRATION OF AN ADULT ATLAS THROUGH INTERMEDIATE TIME POINTS IN CHILDHOOD

Authors *(Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)*

M. Blesa[1], A.F. Serag[1], A.G. Wilkinson[2], E.J. Moore[1], R. Pataky[1], S.A. Sparrow[1], G. Macnaught[3], S.I. Semple[3], M. Bastin[4] and J.P. Boardman[1, 4,*]

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Institution(s)

[1] MRC Centre for Reproductive Health, University of Edinburgh, [2] Department of Radiology, Royal Hospital for Sick Children UK, [3] Clinical Research Imaging Centre, University of Edinburgh, [4] Centre for Clinical Brain Sciences, University of Edinburgh.

Introduction *(include hypothesis)*

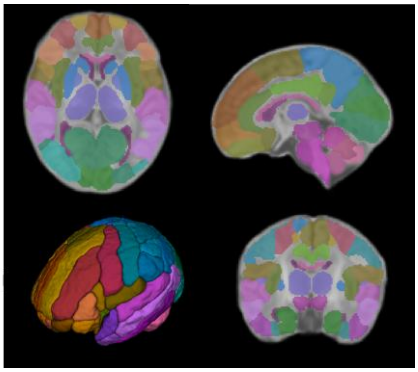
Labelled MRI atlases can be used to: calculate the volume and infer tissue integrity of anatomic regions of interest (ROIs); capture population diversity in brain structure; localise abnormalities; construct growth curves; and to map regional brain growth in response to injury / treatment. Aim: to construct a neonatal atlas with 107 ROIs operable across MRI modalities.

Methods (*include source of funding and ethical approval if required)*

Participants: 25 healthy control infants born at term underwent multimodal MRI with ethical approval. Framework: Stepwise longitudinal non-rigid registration [1] of a labelled adult brain (SRI24/TZO), via MRI templates from children at 4.5yrs, 2.5yrs and 3 months, to the neonatal template [2]; Propagation of the labelled map from the template to structural MRI data from neonatal cohorts using nonlinear image registration [3]; Construction of multimodal atlas using an iterative averaging-based approach [4, 5]. Label accuracy was assessed by a radiologist (AGW). Accuracy between longitudinal and direct registration from adult to neonatal templates was compared using the Dice coefficient. The study was supported by Theirworld and NHS Research Scotland.

Results

We created a neonatal brain template labelled with 107 anatomic ROIs. Manual editing was required for sub-cortical structures, and 17 regions were manually added (lateral ventricles, brainstem, cerebellum and corpus callosum). The figure illustrates colour coded ROIs in three planes and volume rendered cortical regions (bottom left).



The computed transformations for constructing the T1-weigthed atlas were used to create T2-weigthed, fractional anisotropy and mean diffusivity average templates, as well as tissue probability maps (CSF, WM, GM and deep GM).

The Dice coefficient was greater for all brain regions after longitudinal versus direct registration between adult and neonatal templates. Average coefficient for all regions with longitudinal registration: 0.726; and with direct registration: 0.421.

Conclusions

We present a neonatal MRI atlas that captures population diversity, has rich anatomic definition (107 ROIs), and can be used to analyse multi-modal MRI scans. We also show that longitudinal registration using spatio-temporal atlases enhances accuracy for modelling brain change across the life-course.

References *(include acknowledgement here if appropriate)*

1: Serag et al. 2012 **2:** Fonov et al. 2009 **3:** Avants et al. 2008 **4:** Guimond et al. 2001 **5:** Joshi et al. 2002

Title (Upper case)

EARLY ECHOCARDIOGRAPHY DOES NOT PREDICT TREATMENT OF PATENT DUCTUS ARTERIOSUS IN EXTREMELY PREMATURE INFANTS.

Authors *(Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)*

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Institution(s)

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Introduction *(include hypothesis)*

The persistence of Patent Ductus Arteriosus (PDA) in extremely preterm infants is a frequently encountered problem associated with increased morbidity and mortality. Identifying infants who are likely to have a persistent PDA may help to target treatment and reduce associated complications with PDA[1].

Methods (*include source of funding and ethical approval if required)*

This study analysed prospectively collected data from a clinical and echocardiographic trial performed in the Neonatal Unit, Royal London Hospital from February 2013 to July 2014. Infants less than 29 weeks gestation were recruited. Echocardiography was performed on day 1 and 3 of postnatal life. PDA size in B&W and colour, velocity of flow in PDA and flow pattern[2] were obtained. Infants were followed up to monitor those who required medical and surgical management of their PDA. Non-parametric tests were performed for analysis of data using SPSS v22. Regional ethics committee approval (Reference 12/LO/1553) and written parental consent were obtained prior to the start of the study.

Results

33 infants have been studied. The median (IQR) gestation was 26(25-27.1) weeks and birth weight 800 (680-945) grams. Of the 33 infants, 13(39%) required medical treatment for PDA and 6(18%) infants received surgical ligation of the PDA. The median (IQR) PDA size in colour was 1.5(1.2-1.8) mm on day 1 and 1.1(0-1.6) mm in colour on day 3. All infants who had surgical PDA ligation were less than 26 weeks gestation and were ventilator dependant. PDA size measurements (B&W and colour) on day 1 and 3, change in ductal size between days 1 and 3, flow pattern/velocity, or PDA measuring > 1.5 mm did not predict if infants would subsequently receive medical or surgical management of the PDA in this cohort. Using stepwise logistic regression, we found that gestation was the only factor that predicted if the infant would subsequently receive medical (p=0.01) or surgical (p=0.025) treatment for PDA.

Conclusions

It was not possible to predict which infants would receive treatment for PDA based on ductal size, change in ductal size, flow velocity or flow pattern in the first three days of life. Gestational age was the only predictor for receiving medical or surgical treatment of the ductus arteriosus.

References *(include acknowledgement here if appropriate)*

[1] Early echocardiographic prediction of symptomatic patent ductus arteriosus in preterm infants undergoing mechanical ventilation. Martin Kluckow and Nick Evans, J Pediatr1995;I 27:774-9
[2] Su et al. Echocardiographic flow pattern of patent ductus arteriosus: a guide to indomethacin treatment in premature infants. Arch Dis Child Fetal Neonatal Ed 1999; 81:F197-F200

Title (Upper case)

FEASIBILITY OF PULSE OXIMETRY SCREENING FOR CRITICAL CONGENITAL HEART DEFECTS IN HOMEBIRTHS

Authors *(Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)*

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Institution(s)

1. Birmingham Women's Hospital NHS Foundation Trust, Edgbaston, Birmingham UK.
2. School of Clinical and Experimental Medicine, University of Birmingham, Birmingham, UK

Introduction *(include hypothesis)*

Congenital heart defects (CHD) are the most prevalent congenital anomaly and an important cause of neonatal mortality and morbidity. Less than 50% of defects are diagnosed antenatally and NIPE examination also misses up to 50%. Pulse oximetry screening is a safe and effective test for the early identification of critical CHD[1]. Since 2008 we have screened all asymptomatic inborn babies at BWH and this was rolled out to include all home births from 1/1/14. We hypothesised that carrying out the screen at 2 hours of age in babies born at home is feasible and would not result in a large number of false positive tests.

Methods (*include source of funding and ethical approval if required)*

We undertook a retrospective analysis of all of the pulse oximetry tests carried out on homebirths between 1/1/14 and 12/5/15 by interrogating the maternity electronic data system.
We recorded the total number of babies screened and then carried out a separate analysis of those babies with a positive screen and those babies admitted from the Community for other reasons, using the Badgernet system.
We also assessed acceptability of pulse oximetry screening among senior midwives from the homecare team.

Results

Ninety babies were delivered at home during the study period and 80 were screened with Pulse Oximetry.
Data from 10 babies was not on the electronic system.
There were two positive screens (2.2% of the total) and two babies who required retesting in line with our protocol and had normal saturations after retesting
Both of the positive screens were admitted to NNU with a significant respiratory illness.
Three babies who had passed pulse oximetry screening were subsequently admitted to hospital after becoming symptomatic. Two of these babies had a self-limiting problem and one baby was diagnosed with meningitis.
No baby was diagnosed with CCHD during the study period.
Screening was acceptable to midwives, was reassuring to both staff and parents and did not increase workload.

Conclusions

Pulse oximetry screening as part of routine homebirth care at 2 hours of age is feasible and reassuring to both midwives and parents.
Screening identified two babies with significant respiratory illness which required admission to hospital.

References *(include acknowledgement here if appropriate)*

1. Ewer AK, Furmston AT, Middleton LJ, et al. Pulse Oximetry as a screening test for congenital heart defects in newborn infants: a test accuracy study with evaluation of acceptability and cost-effectiveness. Health Technology Assessment. 2012; **16**(2), 1366-5278.

Title (Upper case)

CARDIOVASCULAR FUNCTION AND HYPERTENSION IN YOUNG ADULTS BORN PRETERM: AN INTERIM ANALYSIS

Authors *(Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)*

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Institution(s)

[1] Section of Neonatal Medicine, Imperial College London, [2] Division of Surgery, Oncology, Reproductive Biology and Anaesthetics, Imperial College London, [3] Department of Clinical Biochemistry, University of Cambridge

Introduction *(include hypothesis)*

Preterm birth and survival rates are rising globally, with a number of epidemiological studies demonstrating a clinically relevant increase in blood pressure (BP) in children and adults born preterm, compared to those born at term [1]. Ambulatory monitoring is considered a more reliable approach to assessing BP as it is less affected by the anxiety response that accompanies one-off or clinic measurements. Here, we test the null hypothesis that no differences exist in clinic or ambulatory BP readings between ex-preterm and term born young adults.

Methods (*include source of funding and ethical approval if required)*

This study represents an interim analysis of an ongoing BHF funded study “The preterm baby as a young adult” (REC: 12-LO-1053). Young adults (aged 19-27) born either prematurely (PT: <33 weeks gestation) or at term (T: 39-42 weeks gestation) attended for a single visit. A digital sphygmomanometer was used to measure BP after subjects had rested in a seated position for 5min. An average of 2-3 readings was used to calculate clinic systolic (SBP) and diastolic blood pressure (DBP). Ambulatory monitoring was obtained over 24h using a digital monitor. The difference between clinic and “day” ambulatory BP measures was calculated for each individual.

Results

Data was extracted from for 78 individuals (39 PT (27F); 39 T (23F). Ex-preterm adults demonstrated significantly increased SBP (PT: 127.2 ± 8.8mmHg; T: 118.6 ± 7.0mmHg, $p<0.001$) and DBP (PT: 76.6 ± 8.4mmHg; T: 72.7 ± 7.8mmHg, $p=0.03$) compared to term born controls, with no differences in ambulatory BP. Both female and male ex-preterms demonstrated significantly greater SBP compared to their respective term born controls (Female PT: 125.6 ± 7.5mmHg; Female T: 118.0 ± 7.6mmHg, $p<0.001$; Male PT: 131.3 ± 10.4; Male T: 119.4 ± 6.0, $p<0.001$). Female ex-preterms also presented increased DBP compared to their term born controls ($p<0.01$). The difference between clinic and ambulatory blood pressure was significantly increased in ex-preterm women compared to their term born counterparts (SBP: F PT: 10.9 ± 7.4mmHg, F T: 4.8 ± 7.5mmHg, $p<0.01$; DBP: F PT: 5.5 ± 8.0; F T: -0.4 ± 6.2mmHg, $p<0.01$) with no differences observed in men.

Conclusions

These interim data support previous studies reporting increased clinic SBP and DBP in ex-preterm individuals, with no differences in ambulatory blood pressure [1]. These results corroborate smaller, female only studies [2] demonstrating female ex-preterm adults show an increased BP response to the anxiety of clinical BP measurement. Together with previous studies indicating gender specific trajectories in outcomes of preterm birth [3], these data indicate that future studies examining the long-term effects of preterm birth should be sufficiently powered to detect sex-specific effects.

References *(include acknowledgement here if appropriate)*

[1] Parkinson JR *et al.* (2013) Pediatrics 131(4):1240-1263.
[2] Kistner A *et al.* (2005) Pediatric Nephrology. 20(2):232-233.
[3] Thomas EL *et al.* (2011) Pediatric Research 70(5):507-512.

Title (Upper case)

Nutritional Evaluation and Optimisation in Neonates (NEON): a randomised double-blind controlled trial of amino-acid regimen and intravenous lipid composition in preterm parenteral nutrition

Authors *(Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)*

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Introduction *(include hypothesis)*

Parenteral nutrition is central to the care of very immature infants. There is continuing uncertainty regarding optimal amino-acid intakes and intravenous lipid formulations. High amino-acid regimens and fish oil-containing lipid emulsions have been advocated.

Methods (*include source of funding and ethical approval if required)*

We conducted a two-by-two factorial, double-blind multi-centre randomised controlled trial comparing the effect of immediate delivery of current Recommended Daily Intake of parenteral amino-acids (Imm-RDI) versus incremental introduction (Inc-AA) on body composition, and SMOFlipid versus Intralipid on Intra-Hepato-Cellular Lipid (IHCL). We commenced trial interventions and milk feeds within 24 hours of birth. The trial was pre-registered (ISRCTN29665319; EudraCT: 2009-016731-34) and approved by the UK National Research Ethics Service and Medicines and Healthcare and products Regulatory Agency. The trial sponsor was Imperial College London and was funded by the Efficacy and Mechanism Progamme of the National Institute of Health Research.

Results

We randomised 168 infants <31 weeks gestation. We evaluated outcomes at term in 133 infants. There were no significant differences between Imm-RDI and Inc-AA on non-adipose mass (adjusted mean difference; 95% CI: 1.0g; -108, 111) or between SMOFlipid and Intralipid on IHCL (adjusted mean ratio SMOFlipid:Intralipid; 95% CI: 1.1; 0.8, 1.6). Imm-RDI infants were more likely than Inc-AA to have blood urea nitrogen levels greater than 7mmol/l (75% vs 49%; p<0.01) and 10mmol/l (49% vs 18%; p<0.01) and a smaller head circumference at term (-0.8cm; -1.5, -0.1; p= 0.02). There were no significant differences in any other pre-specified secondary outcomes including adiposity, liver function tests, weight, length or mortality.

Conclusions

Immediate delivery of RDI of parenteral amino-acids does not benefit body composition or growth to term and may be harmful; SMOFLipid does not reduce IHCL. High amino-acid intakes should be used with caution in very preterm neonates and only in the context of randomised controlled trials.

Title (Upper case)

USING NORMALIZATION PROCESS THEORY TO IMPLEMENT AND EMBED IMPROVED NUTRITIONAL PRACTICES INTO THE ROUTINE CARE OF PRETERM INFANTS IN NEONATAL INTENSIVE CARE

Authors *(Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)*

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Introduction *(include hypothesis)*

The nutritional care of preterm infants is often variable and nutrient intakes suboptimal, despite increasing literature regarding best practice in this area, suggesting a failure to translate this into routine care. Using current available evidence for practice, we developed a complex (multifaceted) intervention aimed at optimising nutrient intakes and growth. In order to embed ('normalise') the new practices into routine care, we used Normalization Process Theory (NPT), a novel sociological framework, to develop and guide implementation.

Methods (*include source of funding and ethical approval if required)*

We developed a complex intervention to improve the nutritional care of preterm infants (born <30 weeks or 1500g) and introduced this in a phased manner: Phase 1 (Control period, Jan-Aug 2011); Phase 2 (Partial Implementation, with improved parenteral and enteral nutrition solutions, nutrition team, staff education, Aug–Dec 2011); Phase 3 (Full implementation, with guidelines, screening tool, 'nutrition nurse champions', Jan-Dec 2012); Phase 4 (Post implementation, to assess sustainability of the intervention, Jan-Jun 2013). Bimonthly audits and a staff questionnaire based on NPT were carried out to measure guideline compliance and 'normalisation' of the new practices into routine care respectively. Focus groups and NPT scores were used to guide implementation in real time. Data on nutrient intakes and growth were collected in each phase.

Results

Infant characteristics, mean nutrient intakes and growth in each phase of the study are given in the table below. There were significant improvements in protein intake in phases 2 and 3 compared to phase 1 (both $p<0.001$), and this was sustained beyond the intervention into phase 4 ($p<0.01$ vs phases 1 and 2). There was a significant improvement in the change in standard deviation score from birth (cSDS) for weight in periods 2 and 3 compared to period 1 (both $p<0.01$), which again were sustained post implementation in phase 4 ($p<0.001$ vs phases 1 and 2). There was a non-significant improvement in the cSDS for head circumference (HC) across the study. Mean audit guideline compliance and NPT scores both increased in a linear fashion over time, ($r=0.86$ and 0.15, $p<0.03$ for both), with a significant linear association between the two ($r=0.22$, $p<0.01$).

Phase	n	Mean (SD) Birth weight (kg)	Mean (SD) Gestational Age (weeks)	Mean Daily Energy Intake (kcal/kg/day)	Mean Daily Protein intake (g/kg/day)	Mean Weight cSDS	Mean HC cSDS
1. Control Period	52	1.08 (0.27)	29.2 (2.6)	114	2.87	-0.94	-1.06
2. Partial Implementation	36	1.03 (0.31)	29.2 (2.9)	115	3.09	-0.69	-0.91
3. Full Implementation	75	1.00 (0.27)	28.7 (3.0)	117	3.20	-0.51	-0.74
4. Post Implementation	35	0.92 (0.26)	28.1 (2.8)	120	3.34	-0.39	-0.65

Conclusions

Both the partial and full implementation of the intervention was associated with improvements in protein intake and weight gain which seemed to be sustained beyond the main implementation period. Measures of 'normalisation' using NPT can be related to real measures of clinical practice, suggesting that NPT offers an effective way of implementing new practices that it may lead to sustained changes in practice. This study also suggests that complex interventions based on current evidence have potential to improve practice and outcomes

References *(include acknowledgement here if appropriate)*

Title (Upper case)

Infant feeding at 3 months of age in a prospective cohort born in a WHO baby friendly hospital: the relationship with mode of delivery.

Authors *(Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)*

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Introduction *(include hypothesis)*

We have previously presented evidence that pre-labour Caesarean section (PLCS) is strongly associated with lower breastfeeding initiation[1]; however, independent UK data on infant feeding at 3 months of age are sparse. Here we report method of feeding at 3 months post-partum in infants born in a WHO baby friendly hospital; we use these data to test the hypothesis that feeding 3 months post-partum is associated with mode of delivery.

Methods (*include source of funding and ethical approval if required)*

In February 2014 we commenced recruitment of a prospective cohort of babies born by vaginal delivery (VD), pre-labour Caesarean section (PLCS) and in-labour CS (ILCS) to examine the association between mode of birth and atopy at 1 year of age (Research Ethics Approval 13/LO/1793). Babies were recruited on the post-natal ward at Chelsea and Westminster Hospital following informed maternal consent. We recorded data on feeding prior to discharge and at 3 months post-partum we telephoned mothers to obtain follow-up information. We categorised infant feeding as 1) exclusively breast-fed (EBF); 2) mixed feeding (MF); 3) exclusively formula-fed (EFF). Method of feeding at hospital discharge and at three months was compared between mode of delivery groups using Chi-square tests.

Results

We have to-date recruited 321 infants (VD=107; PLCS=107; ILCS=107) and have obtained follow-up data on feeding at age 3 months on 256 (VD=84; PLCS=85; ILCS=87). At hospital discharge 12.5% of the cohort had received some formula milk, but use of formula prior to discharge was similar across the three delivery groups (VD 8.3% of babies received formula; PLCS 17.2%; ILCS 11.8%; p=0.21). By three months 23.4% overall were EFF; 44.1% EBF and 32.4% MF. Mode of delivery had a significant impact on breastfeeding at 3 months, with babies born by PLCS being more likely to be EFF (VD 17.9%; PLCS 31.0%; ILCS 21.2%; p=0.03). Of the 60 EFF babies fed at 3 months, 19 received some formula milk before discharge but only one was never breastfed; breastfeeding ceased during the first week in 11%, and around the 2nd post-partum month for the majority.

Conclusions

PLCS is associated with an increased rate of EFF at 3 months in babies born in a WHO baby friendly hospital. Mothers delivering by PLCS may require additional breast feeding support. We found an EBF rate at 3 months postpartum more than double that in the 2010 NHS Infant Feeding Survey (national average of 17%). Additionally, given that our cohort was selectively recruited so that 67% of births were by CS (normal CS rate in the hospital is 33%), which is associated with increased EFF at 3 months, 44.1% is likely to be an underestimate of the rate of EBF at 3 months. It is unclear whether this high rate of EBF at 3 months reflects population characteristics or the impact of adherence to the WHO baby friendly hospital initiative. These conclusions have the caveats of maternally reported feeding data, but the strengths of an independent prospective cohort.

References *(include acknowledgement here if appropriate)*

[1] Prior E, et al. (2012) *Am J Clin Nutr* **95**:1113-1135.

Title (Upper case)

EARLY NUTRITION AND NEURODEVELOPMENTAL OUTCOMES IN PRETERM INFANTS: A SYSTEMATIC REVIEW

Authors *(Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)*

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Introduction *(include hypothesis)*

Infants born very preterm are at risk of adverse neurodevelopmental outcomes, and this has been associated to some extent with growth and nutrition during the neonatal period. The effects of higher nutritional intakes on neurodevelopmental outcomes is unclear. We conducted a systematic review in order to examine the effects of either increased parenteral nutrition (PN), enteral nutrition (EN) or both during the neonatal period on neurodevelopmental outcomes in infants born at <32 weeks of gestation or weighing <1501g at birth.

Methods (*include source of funding and ethical approval if required)*

Medline, Embase, CINAHL, HMIC and “Web of science” were searched electronically, with selective citation and reference searching. Included studies had to have provided increased nutrition during the neonatal period and carried out neurodevelopmental or cognitive assessment at toddler age or later childhood. Details on nutritional interventions and neurodevelopmental outcomes were extracted. Meta-analysis and meta-regressions were conducted where appropriate.

Results

Fifteen trials and 4182 infants (1760 = intervention group, 2422 = control group) were included. Four trials examined the effect of increased PN, nine trials examined the effect of EN and two trials looked at both. Meta-analysis was carried out on the most consistently reported outcomes, including the subscales of the Bayley Scales of Infant Development II (BSIDII) at 12-18 months and 24 months corrected gestational age (CGA). Meta-analysis of the PN trials demonstrated a significant decrease in the Mental Developmental Index by 3.99 points (-7.69, -0.29; p=0.03) in the intervention group compared to the control group at 24 months CGA. Results at 12-18 months revealed no significant effect on neurodevelopmental outcomes from enhanced EN or PN. Overall, an increase in nutrition during the neonatal period was not shown to cause significant harms.

Conclusions

The effects of early enteral nutrition on neurodevelopmental outcomes in infants born very preterm and/or with very low birth weight remains unclear, but this review showed that increased early PN may cause unfavourable neurodevelopmental outcomes. While the meta-analysis from this systematic review was limited by the heterogeneous interventions and outcome measures across the trials, such findings require confirmation from further research. Future studies should focus on including standardised nutritional interventions and using a set of agreed and standardised neurodevelopmental outcome measures to provide stronger and more conclusive evidence.

References *(include acknowledgement here if appropriate)*

Title (Upper case)

EPICARDIAL FAT IS A NUTRITIONALLY REGULATED DEPOT OF BROWN ADIPOSE TISSUE NEWBORN INFANTS AND CHILDREN

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Introduction *(include hypothesis)*

Suboptimal nutrition in early life induces metabolic adaptations that may confer short-term survival advantages but are detrimental in later life[1]. Brown adipose tissue (BAT) has a unique role in energy homeostasis and a potential role in lipid and glucose metabolism. BAT activation is a mechanism against excess weight gain and can increase clearance of lipids and glucose. Epicardial fat is anatomically and clinically related to cardiac function and modulates the evolution of cardiovascular pathologies. We have previously shown that BAT is present in adipose tissue depots around the heart in fetal[2] and newborn[3] sheep, and in adult humans[4], and that BAT development in early life is affected by suboptimal maternal nutrition during pregnancy, at least in sheep[2,3]. We hypothesised that epicardial fat is a BAT depot in newborn infants and children and that suboptimal nutrition in early life affects adiposity and BAT development in humans.

Methods (*include source of funding and ethical approval if required)*

With appropriate ethical approvals and informed parental consent, clinical data and epicardial adipose tissue samples were collected from 63 children (0-18y) undergoing cardiac surgery. Anthropometric assessment was performed using the Emergency Nutritional Assessment Tool and the World Health Organisation Antro (v3.2.2). Relative abundance of gene expression for uncoupling protein (UCP)1, the unique BAT protein, and other adipose tissue related genes was measured by microarray analysis. Histology and immunohistochemical analyses of adipose tissue sections were performed to confirm the presence of BAT and UCP1 in this depot.

Results

UCP1 gene was highly expressed in epicardial fat of newborn infants. High levels of UCP1 gene expression was also present in older children and did not change significantly with age.
Among children ≤2y of age, UCP1 gene expression did not correlate with age but was higher in children of Caucasian origin when compared to children of Asian origin (UCP1 mRNA: Caucasian, 10.02 ± 0.48; Asian/mixed, 7.61 ± 0.99 relative signal intensity in arbitrary units (mean ± SEM) $p = 0.02$). Gene expression of UCP1 and leptin (a marker for white adipose tissue) correlated with weight for age z-scores (WAZ) independent of age and gender of the participants (UCP1: $R^2=0.09$; $p<0.05$; leptin: $R^2=0.12$; $p<0.05$). Children with high UCP1 gene expression also had increased expression of other BAT related genes such as DIO2, PPARα and type 3 beta adrenergic receptor but had decreased expression of glucocorticoid receptor gene.
Presence of BAT the epicardial fat depot was confirmed by demonstration of small, multilocular adipocytes that stained positive for UCP1. BAT was demonstrable in all newborn infants and in 23% of older children and adolescents.

Conclusions

Epicardial fat from newborn infants, children and adolescents contains UCP1 confirming that it is a BAT depot in humans. UCP1 gene expression in early years of life in humans is downregulated with poor nutrition. In view of the potential role of BAT in regulation of lipid and glucose metabolism, this may have therapeutic implications for prevention and treatment of cardiovascular complications of obesity.

References *(include acknowledgement here if appropriate)*

1.Ojha, S. et al. (2013), Early Hum Deve, 89:909-13. 2. Ojha, S. et al. (2014), Reprod Fertil Dev. 3. Ojha, S. et al. (2013), Pediatr Res, 74:246-251. 4. Sacks, HS, et al. (2013), J Clin Endocrinol Metab, 98:E1448-55.

Title (Upper case)

A prospective population study of the incidence of severe necrotising enterocolitis in English neonatal units

Authors *(Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)*

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Introduction *(include hypothesis)*

Necrotising enterocolitis (NEC) is a devastating gastrointestinal disease predominantly affecting very preterm infants. The risks of death and long-term morbidities are high, aetiology is uncertain and the variations in enteral feeding strategies are widely believed to influence susceptibility. Here we address the null hypothesis that there is no variation in the incidence of severe NEC (defined as NEC leading to surgery or death) between neonatal networks in England.

Methods (*include source of funding and ethical approval if required)*

We conducted a two-year, national population surveillance study of severe NEC (UKNC-NEC study). We extracted information from the National Neonatal Research Database that contains detailed extracts from the Electronic Patient Records of all admissions to neonatal units in England. These data were verified with local study leads. We used multivariable logistic regression to identify patient characteristics associated with severe NEC. We calculated the unadjusted and adjusted incidence and the ratio of observed to predicted number of cases for each neonatal network and depict this graphically using funnel plots.

Results

All regional networks (n=23) and neonatal units (n=163) in England participated. During the two year period 2012-13, 118,071 infants were born and admitted to neonatal care; 529 died or received surgery for NEC (461 <32 weeks GA). Of infants that received surgery 33.0% (139/421) died. The incidence of severe NEC per 1000 admissions was highest for infants born 24 weeks (112.4, 95% CI 90.0 to 134.8). Low gestational age and growth restriction were significant independent predictors of severe disease. The unadjusted funnel plot for infants born <32 weeks illustrates that the network-level variation in severe NEC rates is consistent with the pattern we would expect if the population rate of NEC is 3.07%. Two of twenty three networks fall just outside the 95% control limits, which may be expected if all variation in NEC cases at network level is due to chance rather than systematic differences between networks. Adjusting NEC rates for birth weight SDS, gestational age and antenatal steroids using a logistic regression model did not affect this conclusion.

Conclusions

We have shown no unusual variation in the incidence of severe NEC at network level in England. NEC is now a cardinal cause of death among very immature neonates; the low incidence rates call for national and international collaboration to test preventive stratagems in adequately powered randomised trials.

References *(include acknowledgement here if appropriate)*

Title (Upper case)

CROSSOVER STUDY OF PROPORTIONAL ASSIST VERSUS ASSIST CONTROL VENTILATION IN INFANTS WITH EVOLVING OR ESTABLISHED BPD

Authors *(Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)*

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Introduction *(include hypothesis)*

During assist control ventilation (ACV), ventilator inflations are triggered by the onset of the infant's respiratory efforts. In contrast, during proportional assist ventilation (PAV) ventilator pressure is servo controlled throughout each respiratory cycle. In addition, the ventilator can provide inflation pressure in phase with the tidal volume change in order to reduce the compliance load (elastic unloading) and in phase with the flow volume change to reduce the resistance load (resistive unloading). We have previously demonstrated in a one hour cross over period study PAV compared to ACV was associated with a significantly lower work of breathing and oxygenation index and higher respiratory muscle strength [1]. We, therefore, hypothesized that PAV compared to ACV would result in a higher oxygenation index over a four hour period, the longest time PAV has been studied in vivo.

Methods (*include source of funding and ethical approval if required)*

A randomised crossover study in prematurely born infants, ventilator dependent beyond the first week after birth was undertaken. Prior to the start of each study, the infant's compliance was determined using the results from the Stephanie ventilator, which delivered both ACV and PAV. During PAV, 100% elastic unloading was used. At the end of each four hour period on ACV and PAV, the oxygenation index was calculated. The planned sample size was 18 infants to allow a detection between the two ventilator modes of a difference equivalent to 0.7 SD in the oxygenation index with 80% power and a two sided significance of 5%.

Results

Infants with a median gestational age 25 (range 24-33) weeks were studied at a median postnatal age of 19 (range 10-105) days. Their median baseline compliance was 0.4 (range 0.3-1.1) mls/cmH_2O and resistance was 155 (range 66-252) cmH_2O/l/sec. Recruitment was stopped at eight patients, as all their OI results were in favour of PAV (p=0.004). The median FiO_2 (p=0.049), the median mean airway pressure (p=0.012) and the median oxygenation index (p=0.012) were all lower on PAV.

Conclusions

These results suggest that PAV compared to ACV is advantageous for prematurely born infants with evolving or established BPD.

References *(include acknowledgement here if appropriate)*

1. Bhat, P., et al. Crossover study of proportional assist versus assist control ventilation. Arch Dis Child Fetal Neonatal Ed, 2015. 100(1): F35-F38.

Title (Upper case)

INVESTIGATING THE INTERACTION OF SP-A AND SP-D WITH RESPIRATORY SYNCYTIAL VIRUS FOR THE DEVELOPMENT OF THERAPEUTIC TREATMENT OF PREMATURE NEONATES.

Authors *(Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)*

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Introduction *(include hypothesis)*

Respiratory syncytial virus (RSV) is the leading cause of bronchiolitis and hospitalisation of infants in developed countries. Surfactant proteins A and D (SP-A and SP-D) are important innate immune molecules present throughout the airways, particularly in pulmonary surfactant which covers the alveolar epithelium. SP-A and SP-D bind carbohydrates on the surface of pathogens to enhance their neutralisation, agglutination and clearance. Moreover they are important modulators of the inflammatory immune response. The aim of this work was to delineate the interaction of SP-A and SP-D with RSV and their capacity to prevent infection of human cells.

Methods (*include source of funding and ethical approval if required)*

Immortalised human bronchial epithelial cells (AALEB) were infected for 2 hours with a clinical strain of RSV A, which had either been incubated with or without different concentrations of SP-A or SP-D. The virus was left to replicate for 24 hours. RSV infection and replication was determined using RT-qPCR.

Results

Pre-incubation of RSV with both SP-A and SP-D reduced levels of infection of AALEB cells in a dose dependent manner. Pre-incubation with 10µg/ml of SP-A decreased infection of RSV by 57.8% (n=3, $P<0.01$). Pre-incubation with 10µg/ml of SP-D decreased infection of RSV by 53.7% (n=3, $P<0.01$). The capacity of SP-A and SP-D to bind RSV attachment (G) and fusion (F) proteins is currently being investigated. Recombinant forms of SP-A and SP-D are also being used to investigate the importance of their oligomeric structure in preventing infection.

Conclusions

Both SP-A and SP-D prevented infection of AALEB cells with RSV A. This may explain the susceptibility of premature neonates with surfactant deficiency to RSV bronchiolitis. Recombinant versions of SP-A and SP-D may have therapeutic potential for the protection of susceptible premature neonates to infection with RSV.

References *(include acknowledgement here if appropriate)*

Title (Upper case)

NEONATAL INTRAVENTRICULAR HAEMORRHAGE DOWNREGULATES NOTCH AND ACTIVATES PROLIFERATION IN THE SUBVENTRICULAR ZONE

Authors *(Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)*

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Introduction *(include hypothesis)*

The clinical outcome and pathological impact of Intraventricular Haemorrhage (IVH) in premature neonates is unclear. It is hypothesised that IVH has the potential to impact on cortical development but evidence in support of this is lacking. Our aim was to design a mouse model that could specifically explore the impact of GMH on the Neural Stem Progenitor Cells (NSPC) within the Subventricular zone (SVZ) and on early cortical development.

Methods (*include source of funding and ethical approval if required)*

Using a modified Narishige stereotactic frame we have optimised and validated a mouse model of Papille Grade II/III GMH. A thymidine labelling strategy on day 1, combined with fluorescent immunohistochemistry at day 4 and day 21 has been used to determine the impact of GMH on postnatal cell division. CD133 MACS sorting at P4 in combination with RNA extraction, amplification and qPCR array has been used to define the impact of GMH on the molecular expression of the neural stem cells within the subventricular zone. Finally in-situ hybridisation has been used to validate targets identified through RNA analysis.

Results

1. Stereotactic injection of autologous blood into the SVZ of newborn mice recapitulates key features of the human condition, namely failure to thrive (weight: control 3.101g ± 0.06, IVH 2.775g ± 0.08, p=0.002) and hydrocephalus (ventricular volume: control 0.054cm^3 ± 0.007, blood injected 0.078cm^3 ± 0.005, p=0.02)
2. GMH leads to an increase in the number of EdU^{+ve} cells within the subventricular zone (cell count: control 59.73 ± 5.53, IVH 160.1 ± 15.18, p=<0.0001) and transcallosal pathway (cell count: control 26.98 ± 1.98 IVH 43.22 ± 3.38 p=0.0004) in association with increased markers of transient amplifying cells (MASH1 (p=0.0009), GFAP (p=0.00002), NG2 (p=0.006, DCX (p=0.003)) consistent with activation of proliferation.
3. RNA analysis from the NSPC (ie CD133^{+ve} cells) at P4 reveals that IVH downregulates Notch expression >25 fold (p=0.01), a finding confirmed by Hes5 ISH.

Conclusions

Notch down regulation may represent a final common pathway following premature birth as such quantification of Notch expression may prove a useful prognostic indicator and raises the possibility that activation of Notch signalling could be a therapeutic strategy for GMH.

References *(include acknowledgement here if appropriate)*

Title (Upper case)

PREPARING FOR HOME: INCREASING PARENTAL KNOWLEDGE, UNDERSTANDING AND CONFIDENCE IN CARING FOR THEIR PRETERM INFANT BEFORE AND AFTER DISCHARGE HOME

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Introduction *(include hypothesis)*

Despite NICE guidance few neonatal units offer structured, family-oriented discharge planning, leaving parents of preterm infants ill-prepared for home, with increased out of hours service use. We implemented a parent-oriented discharge planning approach (Train-to-Home) for preterm infants to investigate the effects on parental self-efficacy scores, infants' length of stay (LOS) and use of healthcare resources in the 8 weeks after discharge.

Methods (*include source of funding and ethical approval if required)*

We included parents of infants of 27-33 weeks gestation during two 11 month periods, before and after implementation of the Train-to-Home in 4 Local Neonatal Units. The parent-oriented package incorporated a train graphic and care pathways to facilitate parents' understanding of their baby's progress, with improved estimation of the baby's likely discharge date. Outcome measures included Perceived Maternal Parenting Self-efficacy (PMPS-E) scores before and after implementing the Train-to-Home together with LOS and healthcare use after discharge.

Results

Parents welcomed the package and reported that the Train-to-Home improved their understanding of their baby's progress, and their preparedness for discharge. There was no significant change in PMPS-E scores for mothers or fathers after implementation of the Train-to-Home, but the number of "out of hours" visits to Emergency Departments (ED) fell from 31 to 20 ($p<0.05$), with a significant reduction in associated healthcare costs (£3400 to £2200; $p< 0.05$) after hospital discharge. There was no reduction in LOS, but in both phases of the study more than 90% of infants went home before their EDD, and more than 50% more than 3 weeks before the EDD. Many nurses felt that the estimated discharge dates were over optimistic, despite being based upon recent local data, and accurately predicting discharge dates for almost 75% of babies in the study.

Conclusions

Despite the lack of measurable effect on the parental self-efficacy scores, the parents reported that their understanding and confidence in caring for their infants were improved by the Train-to-Home, and the reduction in ED attendance and associated costs supports this assessment.

References *(include acknowledgement here if appropriate)*

Funded by a grant (11/1015/09) from the NIHR Health Services and Delivery Research Programme. Ethics approval from NRES Committee London - City & East in June 2012: 12/LO/0944.

Young Investigator Prize: Summary

Title: Parental Influences on Fetal Growth

Fetal growth is influenced by the *in utero* environment and genetic factors inherited from both parents. Poor fetal growth leading to low birth weight is associated with insulin resistance and type-2 diabetes in later life.

My work thus far has investigated the phenotype of parents of pregnancies complicated by fetal growth restriction. Using a case-control study, I showed that men who fathered growth-restricted offspring have pre-clinical insulin resistance and are more likely to smoke than fathers of normal grown offspring. This observation supports the concept that an insulin resistant genotype inherited from a father could manifest as poor fetal growth in offspring.

I, therefore, next investigated the mechanisms through which paternal insulin resistance might be inherited by a growth-restricted fetus. I studied DNA extracted from the cord blood of growth-restricted offspring using whole exome sequencing, identifying novel and rare gene variants in genes associated with maturity onset diabetes of the young (MODY). I validated findings with Sanger sequencing and Taqman genotyping in all family members. I identified rare genes variants in 3 growth-restricted offspring with one of these variants being reported as causative in a MODY individual.
I then studied fetal and placental epigenetics using the Illumina Human 450 BeadChip. I found marked differences in genome wide DNA methylation of fetal cord blood and placental samples from growth restricted compared with normal grown offspring (Epigenetics, 2015), supporting the concept that epigenetic regulation in important in poor fetal growth.

My future work is aimed at investigating the functional consequences of genetic and epigenetic differences to try and identify targets for treatment and prophylaxis against fetal growth restriction and diabetes. My next project will investigate paternal germ line 'sperm' epigenetic changes in the presence of male obesity and type 2 diabetes. We will also be studying offspring born to these fathers to provide evidence for inter-generational inheritance of epigenetic marks associated with growth restriction.

I have also developed an international collaboration with researchers in India and Nepal investigating the impact on fetal growth of hypoxia and whether a fetus' ability to adapt to low oxygen is genetically driven. We will be studying 1200 families (mother, father and offspring) at 4 sites (2 high and 2 low altitude) in India and Nepal.

Title (Upper case)

A RANDOMIZED TRIAL OF VIDEOLARYNGOSCOPY TO TEACH NEONATAL INTUBATION

Authors *(Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)*

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Institution(s)

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Introduction *(include hypothesis)*

Endotracheal intubation is a mandatory skill for neonatal trainees. However, success rates have fallen to <50% amongst junior doctors, largely due to declining opportunities to intubate. Videolaryngoscopy allows the instructor to share the same view of the pharynx as the trainee. We compared neonatal intubations guided by an instructor watching images on a videolaryngoscope screen with the traditional method where the instructor does not have this view.

Methods (*include source of funding and ethical approval if required)*

A randomized, controlled trial at a tertiary neonatal centre recruited from February 2013 until May 2014. Eligible intubations were performed orally on infants without facial or airway anomalies, in the delivery room or neonatal intensive care, by doctors with less than six months tertiary neonatal experience. Intubations were randomized to having the videolaryngoscope screen visible to the instructor or covered (control). The primary outcome was first attempt intubation success rate confirmed by colorimetric detection of expired carbon dioxide.

Results

206 first attempt intubations were analysed. Median (IQR) infant gestation 29 (27-32) weeks and weight were 1142 (816 - 1750)g. The success rate when the instructor was able to view the videolaryngoscope screen was 66% (69/104) compared to 41% (42/102) when the screen was covered, (p<0.001), OR 2.81 (95%CI 1.54-5.17). When premedication was used, the success rate in the intervention group was 72% (56/78) compared to 44% (35/79) in the control group (p<0.001), OR 3.2 (95%CI 1.6 – 6.6).

Conclusions

Intubation success rates of inexperienced neonatal trainees significantly improved when the instructor was able to share their view on a videolaryngoscope screen.

References *(include acknowledgement here if appropriate)*

We would like to thank the infants, their parents and the residents for their participation in the study, the staff at the Royal Women's Hospital and In Vitro Technologies for their lease of the videolaryngoscope for the trial.

Title (Upper case)

***BIFIDOBACTERIUM BREVE* BBG-001 *(B BREVE)* TO PREVENT NECROTISING ENTEROCOLITIS (NEC), LATE-ONSET SEPSIS (LOS) AND DEATH: THE PiPS TRIAL.**

Authors *(Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)*

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Institution(s)

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Introduction *(include hypothesis)*

Necrotising enterocolitis (NEC) and sepsis are important causes of death and morbidity in preterm infants. Administration of commensal bacteria to modify the bowel flora may strengthen intestinal barrier function and prevent NEC and some cases of severe sepsis. Meta-analysis of over 20 published trials of probiotics[1] suggests that probiotics prevent NEC and death, however use is limited. This may be because of lack of robust design and concern about the generalisability of some of the trials.[2]
The aim of the PiPS trial was to test a single bacterial strain probiotic product, *Bifidobacterium breve* BBG-001 to reduce NEC, sepsis and death in an unselected population of preterm babies large enough to give clear results.

Methods (*include source of funding and ethical approval if required)*

The trial was funded by the NIHR through the Health Technology Assessment (HTA) and approved by South Central Oxford A Research Ethics Committee and performed to ICH-GCP. PiPS is a multi-centre double blind randomised placebo controlled trial of *Bifidobacterium breve* BBG-001, 2.1 to 5.3 x 10^8 CFU daily in infants below 31 weeks of gestation, randomised within 48 hours of birth. Colonisation with *B breve* was monitored by culture and PCR of stools at 2w postnatal and 36w postmenstrual age. Primary outcomes were: NEC ≥Bell stage 2, late onset sepsis and death. Results are presented by intention to treat adjusted for sex, gestation, randomisation within 24 hours and allowing for clustering of multiples.

Results

1315 infants were randomised, 5 withdrew, median gestation 28.0w, birthweight 1010g, age starting the intervention 44 hours. No adverse events related to the intervention were reported.

	***B breve*, n=650**	**Placebo, n=660**	**Adjusted RR (95% CI)**
NEC ≥Bell stage 2	61 (9.4%)	66 (10.0%)	0.93 (0.68 to 1.27)
Late Onset Sepsis	73 (11.2%)	77 (11.7%)	0.97 (0.73 to 1.29)
Death	54 (8.3%)	56 (8.5%)	0.93 (0.67 to 1.30)

Analyses of the primary outcomes by subgroups defined by gestational age and birthweight were not suggestive of differential effects in more mature babies and analysis of subgroups defined by colonisation status did not suggest that efficacy was impacted by cross colonisation. Nor were there any differences in a range of clinical and microbiological secondary outcomes.

Conclusions

This probiotic intervention shows no evidence of benefit in this population. This result supports the view that different probiotic strains should be assessed separately and challenges the validity of combining trials using different interventions in meta-analyses.

References *(include acknowledgement here if appropriate)*

1. AlFaleh K, Anabrees J. Cochrane Database of Systematic Reviews 2014, Issue 4.
2. Mihatsch WA et al. Clinical Nutrition 2012;31:e15

Poster Walks

Poster walk A: Thursday 25th June 14.50-15.30

Discussant: Dr Divyen Shah

Paul Cawley, Norfolk and Norwich University Hospital
The thermal safety of neonatal magnetic resonance brain imaging at 3.0 tesla

Therese Ibrahim, Norfolk And Norwich University Hospital
'Feed and wrap' versus routine sedation and use of a vacuum infant immobiliser splint: a review of neonatal brain MRI quality and success in two epochs

M Schreglmann, University Hospital Southampton NHS Foundation Trust
Two-year behavioural and cognitive outcomes of children who underwent therapeutic hypothermia for hypoxic-ischaemic encephalopathy

Nuala Calder, North Bristol NHS Trust
Factors associated with coagulopathy and intracranial bleeding in cooled neonates with hypoxic-ischaemic encephalopathy

Mojgan Ezzati, University College London
Neurotoxicity with dexmedetomidine combined with therapeutic hypothermia in a piglet model of perinatal asphyxia

Poster walk B: Friday 26th June 10.30-11.15

Discussant: Dr Andy Ewer

Jenny Pond, NIHR Southampton Biomedical Research Centre, University Hospital Southampton NHS Foundation Trust
Lost opportunities for nutrition-reasons for missed feeds in a tertiary neonatal unit

Anushma Sharma, Bolton NHS Foundation Trust
Survey of perceptions of withdrawal of intensive care in a neonatal intensive care unit

Mary Pedley, Neonatal Transport Service (NeTS), Portsmouth
Iatrogenic hypocarbia and respiratory alkalosis following neonatal transfer

Nigel Hall, University Hospital Southampton NHS Foundation Trust
Age stratified incidence of gastroschsis

Preethish Shetty, Queen Alexandra Hospital, Portsmouth
Postnatally acquired cmv in extremely premature infants: incidence and clinical manifestations, a single centre 4 year case series

Amy Young, Bradford Royal Infirmary
Co-recruitment in neonatal research; our experience of enrolling mothers and babies in multiple interventional studies

Title

THE THERMAL SAFETY OF NEONATAL MAGNETIC RESONANCE BRAIN IMAGING AT 3.0 TESLA

Authors

Paul Cawley [1], Karen Few [1], Richard Greenwood [2], Paul Malcolm [2], Glyn Johnson [3], Pete Lally [4], Sudhin Thayyil [4], Paul Clarke [1]

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Institutions

1. NICU, and 2. Dept. of Radiology, Norfolk and Norwich University Hospital; 3. Norwich Medical School, University of East Anglia; 4. Centre for Perinatal Neurosciences, Dept. of Paediatrics, Imperial College, London.

Introduction

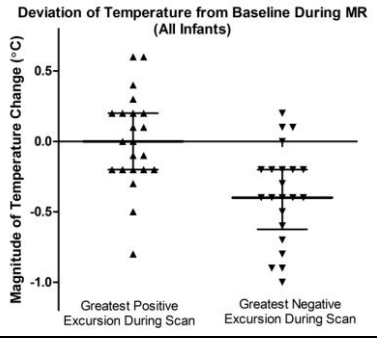
Magnetic resonance (MR) scanning is the gold standard for imaging the neonatal brain. Neonatal MRI has traditionally been undertaken in 1.5 Tesla (T) strength magnetic field scanners, but increasingly 3.0T scanners are being commissioned with the potential for higher quality neuroimaging. Higher radiofrequency energy and use of procedural sedation both have the potential to alter normal thermoregulation[1][2], especially in post-asphyxial neonates. Overheating is dangerous yet data supporting the thermal safety of 3.0T MR scanning in neonates are lacking; indeed no such temperature data were available for our own hospital's 3.0T scanner. We therefore aimed to monitor the core temperature in term neonates undergoing 3.0T MR brain scans in the neonatal period. Our hypothesis was that term neonates undergoing scans in our 3.0T MR scanner would maintain a core (rectal) temperature within the range 36.0-38.0°C during the scan.

Methods

We performed continuous core temperature measurements in consecutively-enrolled term neonates undergoing 3.0T MR brain imaging as part of the MARBLE study (REC ref. 11/H0717/6). All neonates had been treated in our NICU for suspected hypoxic-ischaemic encephalopathy. Rectal thermometry was attained using the MR-conditional FOTS100 fibre-optic temperature system with TSD180 high-accuracy fibre-optic temperature probe (Linton Instrumentation, Diss, UK). MR scans were done with the Discovery MR750w 3.0T scanner (GE Healthcare, UK) and comprised clinical and research sequences (including MR spectroscopy). We recorded vital signs at 5 to 15 minutely intervals throughout the scans. Chloral hydrate was used for sedation. Data were analysed using GraphPad Prism V5 (GraphPad Software, Inc. CA, USA). Paired pre- and post-scan temperatures were compared using Wilcoxon's signed rank test. P <0.05 (2-tailed) was considered significant.

Results

Data were obtained from 22 neonates. Median postnatal age at scanning was 9 days (range: 5-17 days). Median total scan duration was 55 minutes (range: 39-80 minutes). The figure shows maximal individual positive and negative deviations from baseline rectal temperature in the cohort during the scan. There was no significant rectal temperature difference at end of the scan compared with baseline (median pre: 36.8°C [IQR 36.7-37.0°C] vs. post: 36.8°C [IQR 36.4-37.1°C], p=0.16). No infant exceeded a core temperature of 37.5°C during scanning, though minimum temperature fell to <36.0°C (nadir: 35.5°C) in three infants.



Conclusions

3.0 Tesla MR brain imaging using the GE Discovery MR750w scanner does not present a significant thermal challenge to term neonates. These data are reassuring and suggest that routine use of expensive continuous rectal thermometry may be superfluous in this population.

References

1. Isaacson DL et al. *J Magn Reson Imaging*. 2011;33:950-6.
2. Machata AM et al. *Br J Anaesthesia* 2009;102:385-9.

Title

'FEED AND WRAP' VERSUS ROUTINE SEDATION AND USE OF A VACUUM INFANT IMMOBILISER SPLINT: A REVIEW OF NEONATAL BRAIN MRI QUALITY AND SUCCESS IN TWO EPOCHS

Authors

Therese Ibrahim [1], Karen Few [1], Richard Greenwood [2], Cheryl Smith [2], Paul Malcolm [2], Glyn Johnson [3], Pete Lally [4], Sudhin Thayyil [4], Paul Clarke [1].

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Institutions

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Introduction

Successful neonatal Magnetic Resonance (MR) brain imaging relies on a settled infant within the scanner to permit acquisition of the necessary sequences and good quality interpretable images. Unsettledness may lead to incomplete or unsuccessful scans, and sometimes requires costly rescheduling of scans with concomitant anxiety and inconvenience to parents. Significant motion artefact may confound or preclude adequate interpretation and lead to diagnostic errors. Use of premedication to assist neonatal MR scanning is controversial: while routine sedation may be used safely and effectively in neonates,[1] some report successful imaging without routine sedation.[2] It is presently unclear how widely sedation is practised by UK NICUs for MR.

Our NICU introduced routine chloral hydrate sedation and use of a body splint immobilising device for neonatal MR scanning in Nov. 2013 on joining the MARBLE research study. The present study aimed to review our local experience with quality and success of neonatal MR brain scanning in epochs before and after routine sedation and vacuum immobilisation. We also aimed to determine UK practices regarding routine use of sedation for MR.

Methods

We retrospectively reviewed the quality and success of brain MR scans done in Norwich in neonates treated for suspected neonatal encephalopathy since Sept. 2010. We excluded neonates who were intubated during scans and those whose scans were done elsewhere or outside of the neonatal period. Two reviewers (TI and PC) independently reviewed local clinical radiology MR brain scan reports to assess technical quality in two eras: epoch 1 (Sept. 2010-Sept. 2013), when usual practice was 'feed and wrap', i.e. scan after feeding and swaddling the infant; epoch 2 (Oct. 2013-Jan. 2015), when routine chloral hydrate sedation was used along with the Med-Vac™ vacuum infant immobiliser (CFI Medical, MI, USA) for MARBLE study recruits. We devised a simple scoring system to grade scan reports: 0 = no movement artefact mentioned; 1 = minor movement artefact reported radiologically, not apparenty limiting scan interpretation; 2 = significant movement artefact reported, affecting all or most sequences and precluding full interpretation or requiring a rescheduled scan.

In February 2015 we telephone surveyed all tertiary NICUs to ask about use of routine sedation for MR scans.

Results

Baseline characteristics and age at scan were similar. In epoch 2 median scan duration was 55 minutes, ~10 minutes longer than routine clinical scans in epoch 1 (due to extra research spectroscopy acquisition). The table shows scan quality (movement artefact) scores, (Cohen's κ=0.65). Five babies in epoch 1 had seven repeated scans between them due to prior artefacted scans, while none in epoch 2 has needed a repeat scan booking.

Scan quality score:	'Feed and wrap' (n=48)	Sedation & Med-Vac™ (n=23)
0, no artefact, n (%)	23 (48)	23 (100)
1, mild artefact, n (%)	7 (15.5)	0 (0)
2, major artefact, n (%)	18 (38.5)	0 (0)

Of 53 UK NICUs surveyed, 16 (30%) routinely use sedation, 31 (59%) sometimes use, and 6 (11%) never use.

Conclusions

In our centre, routine chloral sedation along with the Med-Vac immobiliser safely achieved a 100% success rate for completed MR scans with good quality images and has proved far superior to the 'feed and wrap' method.

References

1. Finnemore A, et al. *Paediatr Anaesth*. 2014; 24: 190-5.
2. Gale C, et al. *Arch Dis Child Fetal Neonatal Ed*. 2013; 98: F267-8.

Title (Upper case)

TWO-YEAR BEHAVIOURAL AND COGNITIVE OUTCOMES OF CHILDREN WHO UNDERWENT THERAPEUTIC HYPOTHERMIA (TH) FOR HYPOXIC ISCHAEMIC ENCEPHALOPATHY (HIE)

Authors *(Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)*

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Institution(s)

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Introduction *(include hypothesis)*

Therapeutic hypothermia in HIE has been shown to reduce mortality and improve neurodevelopmental outcome into early childhood[1,] Little is known on behavioural outcome and how this is related to cognitive and neurological function and neonatal neuroimaging findings. **Aim:** To describe two-year behavioural and cognitive outcome of newborns who underwent TH for HIE, and to explore associations of behavioural measures with cognitive and neurological function and neonatal MRI findings.

Methods (*include source of funding and ethical approval if required)*

Cross-sectional study in a hospital based cohort of children who underwent TH for HIE and were enrolled into the neurodevelopmental follow-up programme at Princess Anne Hospital Southampton (tertiary neonatal unit). At age two years children were assessed with a structured neurological examination, Bayley Scales of Infant and Toddler Development-III[2], Child Behaviour Checklist 1.5-5 (CBCL)[3], and Checklist for Autism in Toddlers (Q-CHAT)[4]. Neonatal MRI was assessed using the Barkovich scoring system[5]. Data were analysed descriptively and correlations were calculated using Spearman's correlation coefficients.

Results

Thirty-seven children (20 boys), born 09/2009-04/2013, were assessed at a mean corrected age of 28.6 months (range 23-42). Twenty-seven had a normal neurological examination, 4 unspecific signs, 6 cerebral palsy (CP). Mean Bayley cognitive composite score (n=28) was 101 (60-140: SD 15.2). Nine could not be tested due to CP (5), behavioural issues (3), and local follow-up (1). Mean CBCL scores were in the normal range, but a relatively high proportion scored in the subclinical and clinical range for both internalising (20%) and externalizing (39%) problems, in particular attention (32%). Mean Q-CHAT scores were higher than published general population scores (30.1; SD 9.3 versus 25.8; SD 7.7; effect size d = .51); 36% scored in the subclinical (1-2 SD) and 4% in the clinical range (> 2 SD); girls scored higher than boys (33.1; SD 8.5 versus 27.8; SD 9.5; effect size d = .59).
Neonatal MRI findings were associated with neurological status ($r = .698$, $p < .01$), but not with Bayley motor ($r = -.139$, ns) or cognitive scores ($r = -.141$, ns). No association was found between the severity of neonatal MRI or neurological findings and CBCL or QCHAT scores. However, lower cognitive Bayley scores were associated with higher QCHAT ($r = -.528$, $p = .012$), CBCL internalizing ($r = -.550$, $p = .008$), externalizing ($r= -.472$, $p = .026$) and total problem ($r = -.509$, $p = .016$) scores. Lower Bayley language scores were associated with higher Q-CHAT scores ($r = -.432$, $p = .045$).

Conclusions

Our findings suggest a higher risk for various behavioural problems in this group of children and these appear to be associated with cognitive development, but not with neurological status. Neurological and cognitive outcomes of this HIE cohort were slightly better than published data from randomised controlled trials. Further studies with bigger cohorts and longer-term follow-up are needed to examine in more detail the potential behavioural difficulties and associations with neonatal MRI findings.

References *(include acknowledgement here if appropriate)*

[1]Jacobs et al., 2013; [2]Bayley, 2006; [3]Achenbach, 1991; [4]Allison et al., 2008; [5]Barkovich et al., 1998

Title (Upper case)

FACTORS ASSOCIATED WITH COAGULOPATHY AND INTRACRANIAL BLEEDING (ICB) IN COOLED NEONATES WITH HYPOXIC ISCHAEMIC ENCEPHALOPATHY (HIE)

Authors *(Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)*

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Introduction *(include hypothesis)*

Therapeutic hypothermia (TH) and HIE have been associated with coagulopathy, which can result in ICB[1,2]. In this study, we aimed to describe the incidence of ICB in neonates undergoing TH and to identify factors associated with this adverse outcome. We hypothesised that in neonates undergoing TH more severe HIE would result in a more adverse coagulation profile and therefore a higher risk of developing ICB.

Methods (*include source of funding and ethical approval if required)*

A retrospective case study of 50 term neonates treated with TH as per the Western Neonatal Network guideline over a two-year period (2010-2011) was performed. Data was collected on HIE grade (1-3), clotting (APTT, PT, fibrinogen, FBC), blood product use, co-existing diagnosis including sepsis (CRP, blood culture) and demographics. Cerebral bleeding was diagnosed on MRI at day 7-10 (MRI performed in 48/50 patients). Logistic regression models were performed to identify factors independently associated with ICB.

Results

HIE grade 1 was seen in 16% of neonates, HIE grade 2 in 58% and HIE grade 3 in 26%. ICB was diagnosed on MRI in 19% (9/48). Prevalence of co-existing diagnosis was as follows: placental abruption in 16%, persistent pulmonary hypertension in 18%, placental insufficiency in 2% and sepsis (defined as CRP > 10 mg/l) in 66%. Severity of HIE was associated with higher PT ($p = .01$), with lower fibrinogen ($p = .03$) and with lower platelet count ($p = .01$). More severe HIE grade was also associated with an increased risk of ICB (odds ratio 7.3, $p = .009$). In logistic regression models including co-existing condition, gender and HIE grade, placental abruption was independently associated with ICB ($p = .02$). Furthermore, placental abruption was associated with higher APTT and PT, independently of HIE grade (both $p = .001$). The association between HIE grade and ICB was stronger after adjusting for gender and doses of coagulopathy-correcting blood products (odds ratio 28.3, $p = .03$).

Conclusions

Severe HIE is associated with more adverse coagulation parameters and therefore with higher risk of ICB. In addition, our study found that placental abruption is independently associated with coagulopathy and risk of ICB. Further work is required to confirm this relationship and explore potential mechanisms.

References *(include acknowledgement here if appropriate)*

(1) Castle V, Andrew M, Kelton J, Giron D, Johnston M, Carter C. Frequency and mechanism of neonatal thrombocytopenia. J Pediatr 1986 May;108(5 Pt 1). 749e55. **(2)** Forman KR et al. Coagulopathy in newborns with hypoxic ischemic encephalopathy (HIE) treated with therapeutic hypothermia: a retrospective case-control study. *BMC Paediatrics* 2014, 14:277

Title (Upper case)

NEUROTOXICITY WITH DEXMEDETOMIDINE COMBINED WITH THERAPEUTIC HYPOTHERMIA IN A PIGLET MODEL OF PERINATAL ASPHYXIA

Authors *(Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)*

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Introduction *(include hypothesis)*

Despite therapeutic hypothermia, ~ 50% treated babies have adverse outcomes (1); Adjunct therapies are needed. There are strong evidence for associations of perinatal inflammation and infection with neonatal encephalopathy (NE) (2). Dexmedetomidine, a highly selective α2-adrenoreceptor agonist, has analgesic, sedative, anti-inflammatory, and organ-protective properties (3). We aimed to determine if combination of Dexmedetomidine and hypothermia is neuroprotective after cerebral hypoxia-ischaemia (HI) in a piglet model.

Methods (*include source of funding and ethical approval if required)*

*UK Home Office Guidelines [Animals (Scientific procedures) Act, 1986]. After HI, randomisation to: i) Cooling (n=10) or ii) Cooling + Dexmedetomidine (n=10) .In Dex group, a loading dose of Dex at 10 min post resuscitation followed by a maintenance dose for 48 hours. Fentanyl was substituted by Dex in Dex group while continued in Cooling group. MRS was acquired at 24 & 48 h; NIRS at baseline and up to 1h after HI; regional cell death by immunohistochemistry and plasma levels of Dex were measured.

Results

Plasma Dex levels were below 1mcg/L in most piglets. Irrespective of Dex plasma levels, the Dex group had significantly more bradycardia, hypotension, cardiac arrests and higher lactate levels requiring more fluid resuscitation (p=0.05). There was significantly lower Heart Rate (HR) and lower cerebral total haemoglobin (Δ[HbT]) compared to baseline in Dex group following dexmedetomidine loading dose ($p<0.05$). There was no difference in thalamic Lactate/NAA (p=0.66), white matter Lac/NAA (p=0.21) and whole brain NTP/epp (p=0.73) ratios over the 48h after HI between both groups. The overall cell death across all brain regions was significantly increased in the Dex group versus controls (p=0.019).

Conclusions

Dex with cooling was neurotoxic following HI in our piglet perinatal asphyxia model. The Dex group had more fatal cardiac arrests despite blood Dex levels within target sedative range. The Dex group had significantly lower HR and cerebral blood volume (Δ[HbT]) following the loading dose which could explain the neurotoxic effect.

References *(include acknowledgement here if appropriate)*

1- Edwards, A. et al, British Medical Journal, 340**,** c363, 2010. 2- Wang et al., *J Immunol,* 183**,** 7471-7, 2009. Sanders and Maze, *Curr Opin Investig Drugs,* 8**,** 25-33,2007 * Action Medical research grant (SP4553/GN1775)

Title (Upper case)

LOST OPPORTUNITIES FOR NUTRITION- REASONS FOR MISSED FEEDS IN A TERTIARY NEONATAL UNIT

Authors *(Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)*

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Introduction *(include hypothesis)*

It is well described that preterm infants often receive inadequate nutrient intakes during their stay in the Neonatal Intensive Care Unit (NICU). One reason for this is that it is challenging to achieve recommended nutrient intakes enterally, partly due to problems with feed tolerance and difficulties establishing enteral feeds. In order to better understand why feeds are missed or stopped, we explored this using an existing nutritional data set.

Methods (*include source of funding and ethical approval if required)*

We carried out a secondary analysis of detailed nutrition and growth data collected on a cohort of preterm infants born and cared for in our NICU between 2009 and 2012 with a weight of less than 1500g or a gestational age of less than 30 weeks at birth. Daily data was collected for each infant on the type and volume of feeds given, together with the volume of any feeds omitted and the reasons given for omission.

Results

Data was collected on 174 infants: mean (SD) weight of 1.03 (0.29) kg and gestational age of 28.7 (2.8) weeks at birth. In total 18412mls of feed were missed, accounting for 4.3% of total enteral feeds aimed to be given. The main causes of missed feeds, together with the frequency that they occurred and the total volumes of feeds missed are given in the table below. The commonest causes were blood transfusion, concerns regarding nasogastric (NG) aspirates or abdominal distension, extubation or reintubation, and respiratory distress.

Reason	No. of episodes	Total missed (mls)	Mean (mls/episode)
Blood transfusion	274	6210	22.7
Large NG aspirate volume or vomit	312	2960	9.5
Abdominal distension	46	1422.5	30.9
Extubation/reintubation	72	1060.5	14.7
Respiratory distress	37	1033.7	27.9
Other procedure	65	434.5	6.7
Large aspirate and abnormal colour	52	353.5	6.8
Nurse error/workload	12	291	24.3
Bilious/green aspirates	76	284	3.7
Brown/Mucky/Bloody aspirate	27	128	4.7
MBM/colostrum not available	13	55.2	4.2
Other	61	590.3	9.7
No reason given	280	3596.5	12.8

Conclusions

Missed feeds account for a reasonable proportion of the total enteral feeds a baby could potentially receive whist on NICU. While some of these are unavoidable, this work suggests that some missed feed opportunities could be prevented by the introduction of, or changes to, unit policies, such as guidelines for managing feeds in response to aspirates or abdominal distension, or feeding around invasive procedures or periods of respiratory distress.

References *(include acknowledgement here if appropriate)*

Title (Upper case)

SURVEY OF PERCEPTIONS OF WITHDRAWAL OF INTENSIVE CARE IN A NEONATAL INTENSIVE CARE UNIT

Authors *(Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)*

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Institution(s)

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Introduction *(include hypothesis)*

Decisions about end of life care are difficult and differences of opinion exist between professionals. Following a critical incident in a baby where care had been reoriented, we decided to produce more rigorous agreed documentation to record the plans for resuscitation in such babies in NNU. Before formulating such a document, we wanted to explore views about this aspect of care amongst the multidisciplinary team involved. Although there are data in the nursing and medical literature, no published multidisciplinary articles were identified.

Methods (*include source of funding and ethical approval if required)*

A survey of 8 questions was piloted. After Trust R&D approval, in May-June 2013 all nursing and medical staff members on the unit were presented with the anonymous questionnaire, in person by 2 nurses and a registrar at the beginning of the shift and completed questionnaires were collected at the end of the day. The questions were aimed to explore the personal views about whom to consider for reorientation and whether religious beliefs/personal experiences influenced the decision making process. There was allowance for free text to qualify for the yes/no responses which was used widely.

Results

Survey was completed by 18 doctors and 119 nurses. There was 100% return rate of questionnaires. It was noted that some questions were not answered by a significant proportion of responders (e.g. what does DNR mean to you and the optimum timing of discussions about palliative care). This is probably because individuals felt uncomfortable with these responses. 85-89% surveyed considered DNR for patients with very little hope of survival for more than a week. 89% doctors versus 56% nurses considered DNR for patients whose quality of life is poor but may survive for months/years. 40% surveyed thought doctors had right to override decision of the family about DNR. 88-96% participants felt need for an individualised plan for limitation of care on NNU and felt that patients were not likely to be neglected once such a plan is formalised. 55% doctors & nurses felt their own religious belief/non-belief could influence their perceptions in this matter.

Conclusions

An individualised plan for limitation of intensive care on our NNU is supported by medical and nursing staff. There is a need for education about ethical and legal aspects of decisions for end of life care. The staff needs to recognise that their own beliefs may influence their decisions when dealing with this emotive area of care.

References *(include acknowledgement here if appropriate)*

1.http://www.bapm.org/publications/documents/guidelines/NICU-Palliative-Care-Feb-2014.pdf
2. Barr P. Neonatologists' end-of-life decisions. Arch Dis.Fetal Neonatal Ed 2007; 92 (2): F104-F107.

Title (Upper case)

IATROGENIC HYPOCARBIA AND RESPIRATORY ALKALOSIS FOLLOWING NEONATAL TRANSFER

Authors *(Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)*

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Introduction *(include hypothesis)*

The transfer of ventilated infants is essential for ongoing intensive care, surgery and specialist opinion. Any assisted ventilation risks hypocarbia, which has been associated with cerebral hypo perfusion and the developmental of periventricular leucomalacia[1]. This study investigated incidence of hypocarbia in infants transferred by NeTS (Solent) in 2013 and to identify associated factors.

Methods (*include source of funding and ethical approval if required)*

Records for all 84 ventilated transfers were reviewed. Detailed analysis was performed on infants with pCO_2 <4kPa or pH >7.45 on arrival at the receiving unit ("hyperventilated" HV group).

Results

68 ventilated day time transfers were undertaken. Two infants had pCO_2 <4kPa and pH >7.45 (16.6%), five infants had pCO_2 <4kPa but normal pH (41.6%) and five infants had pH >7.45 (41.6%).
Reasons for transfer in 12 with HV were as follows: Post-op PDA: 7, Unstable/delivered at DGH: 3, Limb abnormality: 1, Pre-op PDA: 1.

Analysis of results was undertaken to identify infants at risk of HV:

Factor	Group	HV	Not HV	p value * or §
Median gestation at birth		25+1	28+5	
Gestation at birth	<27+6 weeks	9	26	0.06§
	≥28+0 weeks	3	30	
Gestation at transfer	<27+6weeks	2	11	0.03§
	≥28+0 weeks	10	45	
Age in days at transfer	0-6 days	4	28	0.3525*
	≥7 days	8	28	
Ventilation settings adjusted prior to leaving referring unit	Adjusted	4	40	0.0193*
	Same	8	16	
Transfer associated with PDA ligation	Pre-op	1	13	0.0329*
	Post-op	7	7	
Grade of doctor undertaking transfer	Registrar/ ANNP	9	24	0.0356*
	Consultant	1	22	

*by exact Fisher's test §by Mann Whitney U test

16 night time ventilated transfers were undertaken. Two infants had pH>7.45 and no infants had pCO_2 <4kPa. There was no significant difference in HV incidence between day and night time transfers.

Conclusions

17.6% of day time & 12.5% of night time transferred infants were subjected to HV. Infants were significantly more likely to experience HV if transferred by SpR, ventilation setting not adjusted, post-op PDA or transferred at ≥28 weeks gestation. A larger study is necessary to understand the relationship between these factors.

References *(include acknowledgement here if appropriate)*

1. Fujimoto, S. Togari, H. Yamaguchi, et al, Hypocarbia & cystic PVL in premature infants. ADC F&N Ed 1994;**71**:107-10

Title (Upper case)

AGE STRATIFIED INCIDENCE OF GASTROSCHSIS

Authors *(Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)*

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Introduction *(include hypothesis)*

Many reports in the last two decades have documented an increase in the incidence of gastroschisis worldwide.

The association of gastroschisis with young maternal age is well known but has never been quantified.

The aim of our study is to report the incidence of gastroschisis within our region with focus on maternal age during a 20 year period.

Methods (*include source of funding and ethical approval if required)*

For 20 years our region has had a congenital anomaly register. This is run by a consultant clinical geneticist and registers antenatal and postnatally diagnosed congenital anomalies. Maternal demographics are recorded on this register. The number of gastroschisis for the period 1994-2012 were analysed with respect to maternal age. Denominator birth rates for the region were collected from all the hospitals and compared with data from the Office of National Statistics for accuracy. This allowed us to calculate incidences.

Results

In the study period we had 246 cases of gastroschisis out of a total of 524,372 live and still births.

This is an overall incidence of 4.67 cases per 10,000 births. For all ages this equates to a prevalence of 1:2,141. For maternal age <20 years the prevalence was 1:380 and for maternal age >40 years this was 1:16,286.

Only 4 patients had associated chromosomal anomalies. The number of patients each year was static.

Conclusions

Analysis of our congenital anomaly register has allowed us to stratify the incidence of gastroschisis in our region with regard to maternal age. The overall incidence is 1:2,141. For maternal age <20 years this is much higher at 1:380 and for maternal age >40 years this is much lower at 1:16,286.

References *(include acknowledgement here if appropriate)*

No conflict of interest

Title (Upper case)

POSTNATALLY ACQUIRED CMV IN EXTREMELY PREMATURE INFANTS: INCIDENCE AND CLINICAL MANIFESTATIONS, A SINGLE CENTRE 4 YEAR CASE SERIES

Authors *(Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)*

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Introduction *(include hypothesis)*

Postnatal transmission of Cytomegalovirus (CMV) from mother to premature infants, generally via breast milk, is widely reported. We reviewed our experience of postnatally acquired CMV in extremely premature infants cared for in our department over a 4 years period to ascertain the local incidence and clinical manifestations in this population. We also reviewed antiviral use, clinical and virological response and outcome.

Methods (*include source of funding and ethical approval if required)*

The infants with postnatally acquired CMV infection from May 2011 to April 2015 and denominator data were obtained from a search of the BadgerNet® database. Further detailed information about these nine infants was obtained from case notes and laboratory electronic records.
After informed consent, 'spare' neonatal heel prick screening blood spots were sent for CMV Polymerase Chain Reaction (PCR) in 5 of 9 infants. We have not analysed maternal breast milk for CMV from our cohort.

Results

A total of 237 extremely premature infants were admitted during the study period. Nine infants were diagnosed with acquired CMV infection (3.8%). The gestational age range of the CMV infected infants was from 23^{+2} to 26^{+6} weeks and their birth weights ranged from 0.48 kg to 0.98 kg. Six of the infants were male. All nine infants had received maternal breast milk and were diagnosed with CMV infection after 4 weeks of life. CMV PCR was positive in all infants from urine and blood samples. Day 5 blood spots were negative for CMV in 3 infants, 2 further results are pending.

At diagnosis 7 infants had thrombocytopenia, 4 had deranged liver function, 3 had sepsis like syndromes and 1 had neutropenia. Six were treated with Valganciclovir and one with Ganciclovir. Three were managed conservatively. There were no complications documented either with CMV infection or treatment given. Blood counts and liver function normalised within 2 weeks and CMV was undetectable within 4 weeks of diagnosis in all treated infants. Three infants had transient neutropenia ($<1.0x10^9$/L) after treatment with Valganciclovir with 1 infant having neutropenia of $<0.5x10^9$/L.

Of the untreated infants, 2 had isolated thrombocytopenia and were otherwise well. Platelets normalised within 2 and 4 weeks. The third untreated infant had a 'hepatitis' picture, which resolved after 8 weeks.

Conclusions

Postnatally acquired CMV was common in our extremely premature population, possibly related to our high use of maternal milk. Presentations ranged from isolated thrombocytopenia to sepsis like syndromes. CMV infection should be considered in infants with new onset thrombocytopenia, deranged liver function, neutropenia and sepsis like syndromes. We chose to treat babies with apparent CMV related clinical deterioration despite lack of evidence base, but Valganciclovir appeared well tolerated. 'Spare' neonatal screening blood spots can be analysed retrospectively to assess for missed congenital CMV infection. Long term follow-up is recommended.

References *(include acknowledgement here if appropriate)*

Postnatal CMV: innocent bystander or hidden problem? S Luck & M Sharland, ADC F&N Ed 2009;94:F58–F64

Title (Upper case)

Co-recruitment in Neonatal Research; Our Experience of Enrolling Mothers and Babies in Multiple Interventional Studies.

Authors *(Presenting author underlined. If no author is a Society member please provide the name of the member introducing the author to the Society)*

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Introduction *(include hypothesis)*

Having a preterm baby is a stressful experience. Seeking consent for participation in research may add to this. The perceived ethical and scientific difficulties posed by co-recruitment may also dissuade clinicians from approaching parents. We sought to describe co-recruitment to three interventional RCTs running concurrently on our unit, and establish if parental decline of one study reduced the likelihood of participation in others.

Methods (*include source of funding and ethical approval if required)*

We reviewed approach and participation logs of three multicentre trials running concurrently over a 21 month period on our 32-bed tertiary neonatal unit. One RCT tested a perinatal intervention, and two trialled feeding related interventions. We assessed rates of approach, consent and randomization for the longest-running of the three studies and analysed reasons for non-recruitment. A similar population of newborns were eligible for all three studies; those born at <32/40 or weighing <1500g with no significant congenital abnormalities. We limited our analysis to inborn infants.

Results

Over a period of 21 months, 145 babies were eligible for two studies and 21 for three. Recruited infants were less mature than those eligible overall (28 vs 29 weeks $p<0.05$). 57% of parents were approached for consent to the longest-running trial. Reasons for not approaching included 'Time constraints' (40%), 'Clinical decision' (26%), 'Patient factors' (8%) and 'Staffing' (2%). While three studies were open, 67% of 21 were recruited. 14% were in three, 43% in two, and 10% in only one trial. Half those declining an initial trial participated in a second. More of those joining a first trial agreed to join a second (70% vs 48% $p<0.05$). Of parents consenting to a second trial, 64% had declined participation in a first trial.

Conclusions

Whilst parents who declined to participate in an initial study were less likely to consent to subsequent trials, the majority who joined a second had in fact declined a first. Clinicians should not be dissuaded from seeking consent solely on the grounds of initial lack of participation.

References *(include acknowledgement here if appropriate)*

1. Brocklehurst P. Randomised Control Trials in Perinatal Medicine: Recruitment of a Pregnant Woman or her Newborn Child into More Than One Trial. British J of Obs and Gynae. 1997; 104: 765-767.

Self Certificate of Attendance

Please complete the form below and have it signed by a member of the neonatal society committee if you wish to claim RCPCH CPD points

The Neonatal Society Summer Meeting

June 25th – 26th 2015

Name of person claiming CPD points:

(Blockletters)…….

Place of Work:…….

Number of CPD points claimed :……..

(1 point per hour of attendance – up to a maximum of **5 CPD Points per day**)

Claimant's Signature……..

Name and signature of Neonatal Society Committee member

……

Helen Budge/Howard Clark/Richard Thwaites/Neena Modi/James Boardman

Andrew Ewer/Topun Austin/Divyen Shah/David Carr

(please delete as appropriate)