POSTER SESSION 6 - BRAIN 2

SEPTEMBER 16, 2021 – 13:30 – 14:30 CEST

ID 323 - Documentation around the Commencement of Therapeutic Hypothermia for Hypoxic-Ischaemic Encephalopathy (HIE). A Quality Improvement Project. St Georges Hospital, London.

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Background:
Healthcare Safety Investigation Branch (HSIB) have begun to investigate infants who have been 'cooled' for HIE in England. This triggered an audit of electronic records(iCLIP) for infants cooled Jan 2020 to Jan 2021 at St Georges University Hospital SGH), London. Perinatal HIE has a significant risk of long-term neurological and developmental sequelae, HSIB aim to improve quality of care in attempt to minimise these. 1–3.5/1000 births in the UK have perinatal asphyxia severe enough to cause neonatal HIE. Without intervention, risk of death or severe disabilities in survivors of moderate to severe HIE is 25% and 75% respectively. With therapeutic hypothermia, mortality and disability has reduced but it remains an area of interest for quality improvement and litigation.

Objectives:
An audit to identify gaps in the documentation around commencement of therapeutic hypothermia in infants with HIE. This will enable the team to highlight areas that need to be developed to allow more robust documentation in the future therefore improving patient safety.

Methods:
iCLIP entries were examined for; maternal history, delivery details including, resuscitation, cord gases, neurological examination, Cerebral Function Monitoring (CFM), time of cooling, seizures and reasons for early re-warming.

Results:
18 infants were cooled in 12 months. 33% were out born. Two infants were <36 weeks, three had cooling commenced >6 hours of age due to changing neurology, one rewarmed early due to diagnosis of chromosome disorder. One patient died after rewarming. 27% had no maternal history documented, cord pH not mentioned in 27% of cases, 22% had no resuscitation note, 27% did not have the age in hours documented at commencement. 11% of patients had no neurological examination documented prior to cooling. 5% did not have CFM results documented.

Conclusion:
Audit identified good documentation around infants who were cooled outside of cooling criteria. Some deficits were identified around maternal history, resuscitation, neurological examination. These results alongside the HSIB investigation have prompted an update of the HIE Guideline, triggered departmental teaching and production of an electronic pro forma for iCLIP documentation. This will improve and standardise documentation in infants with HIE.

None declared

ID 230 - NEUROMODULIN CONTENT IN BLOOD SERUM IN PRETERM INFANTS WITH PERINATAL LESIONS OF THE CENTRAL NERVOUS SYSTEM IN THE FIRST DAY OF LIFE

Мистер Artyom Andreyev[1], Doctor of Science (Medicine) Natalya Kharlamova[1], Doctor of Science (Medicine) Galina Kuzmenko[1], mrs Irina Popova[1], mrs Anna Pesenkina[1], mrs Elizaveta Kryazheva[1], mrs Vasilisa Sukhanova[1], mrs Daria Tanana[1]

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BACKGROUND.

At the moment, in scientific works, certain neuromarkers of lesions to the central nervous system in newborns have been well studied. The aim of the study was to study the concentration of neuromodulin (GAP-43) in the first day of life in preterm infants and to establish significant correlations with the clinical parameters of preterm infants in the early neonatal period.

METHODS.

We examined 81 preterm infants (weight <1500 grams, gestational age <32 weeks), which were divided into groups depending on the presence of intraventricular hemorrhage (IVH): Group I – 48 preterm infants in whom during observation in the early neonatal period it was verified IVH; Group II – 33 preterm infants without IVH. Determination of the concentration of neuromodulin in the blood serum was carried out by the enzyme immunoassay. The groups were comparable in terms of weight and height indicators, gestational age, degree of respiratory failure at birth, and the need for mechanical ventilation in the NICU ($p<0.05$). Group I had a significantly lower Apgar score at the end of the 1st ($p=0.034$) and 5th minutes of life ($p=0.037$) in comparison with group II.

RESULTS.

A comparative analysis of the concentration of neuromodulin revealed that in children of group I, the values of neuromodulin were statistically significantly higher than in children of group II (1.469 [1.284; 1.966] ng/ml vs 0.541 [0.461; 0.595] ng/ml; $p <0.001$). IVH degree ($r=0.771$; $p<0.001$), minimal aEEG trend amplitude ($r=-0.404$, $p=0.004$), Ballard score ($r=-0.614$, $p=0.019$) statistically significantly correlated with serum neuromodulin concentration blood.

CONCLUSION.

The reference values of neuromodulin in the first day of life in preterm infants with perinatal CNS lesions were established, depending on the presence of IVH and gestational age, and significant correlations between clinical data and the level of the protein under study were revealed.

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ID 526 - PARENTAL ENGAGEMENT AND FEEDBACK ON PARENT REPORT OF CHILDRENS' ABILITIES- REVISED QUESTIONNAIRE (PARCA-R-Q): A FEASIBILITY STUDY

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BACKGROUND
Standardised neurodevelopmental questionnaires offer an alternative to formal resource intensive, face-to-face assessment for high risk NICU graduates. PARCA-R-Q is a validated tool for assessing children's cognitive and language development at 24 months of age and recommended by NICE, UK. Currently there is no data on parental feedback on using this questionnaire. The aim is to gather service user feedback for PARCA-R-Q as a quality improvement and feasibility study.

METHOD
Formal multidisciplinary 2-year neurodevelopmental assessment clinic for infants at high risk for acquired brain injury currently runs in a hybrid model. All parents who completed PARCA-R-Q for this clinic were invited to participate in an anonymised feedback. A 14-items feedback survey was developed locally and co-designed by a parent representative. The survey consisted of open and closed ended questions and explored parents knowledge, language barriers, completion time and ease to complete the PARCA-R-Q. Parental views on the hybrid clinic model were explored. An electronic link to the feedback was sent after verbal consent. Second reminder was sent by email or text message.

RESULTS
13 parents completed the feedback. 75% were preterm, 78% spoke English as their first language and 78% completed the PARCA-R-Q before attending the developmental clinic. 89% of the PARCA-R-Q was completed by mothers and 11% needed aid from healthcare professionals. 67% preferred face to face formal assessments while only 22% preferred PARCA-R-Q. 67% thought the PARCA-R provided ideas encouraging their child's developmental growth. However 45% thought that the questionnaire needs improvement and is only somewhat useful.

CONCLUSION
The implementation of PARCA-R questionnaire has been a positive change, empowering parents/guardian in the assessment of their child and provides them with ideas to boost child's development. However a significant number preferred face to face formal assessments. This is the first pilot data on parental feedback on the PARCA-R-Q. Further data with a larger cohort is needed to quantify the results.

NONE DECLARED

ID 20 - ENCOURAGING NEONATAL-MATERNAL BONDING: REDUCING SEPARATION DUE TO BORDERLINE CORD GASES

Doctor Emma Bailey[1], Doctor Spandana Madhabushi[1], Doctor Prathiba Chandershaker[1]
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Background:
Poor cord gases are a well-known indicator of poor neurological outcomes in neonates, on which NICE Guidelines for Therapeutic Hypothermia are based. Currently, any baby with a cord gas pH <7.0 meets 'Criteria A', therefore any abnormal neurology ('Criteria B') noted can result in the infant being cooled for 72 hours to reduce long-term neurological injury.
Routine practice in East and North Hertfordshire Trust's Neonatal Unit prior to 2019 was to admit and perform 12 hours of neurological observation on any baby with cord gas pH <7.05, i.e. above the NICE threshold. A drawback of this is that otherwise well term babies are separated from their mothers for prolonged periods solely on the basis of cord gases, thus reducing neonatal-maternal bonding. In this study, the potential to reduce admissions of otherwise well babies with borderline cord gases is explored.

Method:
BadgerNet, a program used to store information on all Neonatal Unit Admissions, was used to search for infants who were >37 weeks' gestation and admitted due to poor cord gases over a year period from 2018 to 2019. These infant records were then reviewed, and their cord gases and neurological observations collated.

Results:
From our search we found 27 infants were admitted to the Neonatal Intensive Care for 12 hours of observations. Of these infants, only 1 went on to have abnormal neurology at 24 hours of age, after the observations had stopped (see Table 1).

Review of the infants with cord gas pH <7.00 showed 21% had no other reason for admission, i.e. they did not require intravenous fluids or respiratory support. Comparing this to the infants with cord gases between pH 7.00-7.05, this number increased to 69%.

Conclusion:
Over a period of a year, we found the majority of babies admitted due to borderline cord gases remained well and required no intervention. Accordingly, a change in practice which allows infants with cord gases between pH 7.00-7.05 to be monitored in transitional care, rather than being admitted to NICU, has been made. This represents an effective trade-off between clinical safety and promotion of neonatal-maternal bonding.

	pH <7.00	pH 7.00-7.05
Normal neurology	13	13
Abnormal neurology	1*	0
*This baby who was admitted due to abnormal cord gases developed seizures at 24hours of age (after the neurological observations had stopped). On further investigations (including MRI) was found to have mild to moderate HIE.		

Table 1: Table to show the number of infants admitted to the NICU for neurological observation due to poor cord gases that went on to have normal or abnormal neurology

None declared

ID 111 - THE ASSOCIATION OF NUCLEATED RED BLOOD CELLS WITH INTRAVENTRICULAR HEMORRHAGE AND EARLY MORTALITY IN VERY LOW BIRTH WEIGHT INFANTS

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Background:
Nucleated red blood cells (NRBC) are progenitores of red blood cells that are physiologically seen in the peripheral blood of the fetus and newborn at birth. The increased numbers of NRBC in the circulation is associated with pathologic conditions such as prematurity, intraventricular hemorrhage, intrauterine growth restriction or death.

Objective:
To determine the association of NRBC levels at NICU admission (day 1) with intraventricular hemorrhage (IVH) and early mortality in very low birth weight (VLBW) infants.

Methods:
Premature infants with a gestational age <32 weeks and a birth weight <1500 g born in a single center within a six month period were evaluated. We assessed the association between absolute NRBC count on day 1 of life and any grade IVH also the composite outcome of IVH and early mortality (death within the first week of life) in this cohort study.

Results:
In the study, data of 98 infants were analyzed. The mean (±SD) gestational age and birth weight of the study group were 28 (±2) weeks, 1043 (±283) g; respectively.
A total of 17 (17.5%) infants developed IVH. Median absolute NRBC count was significantly higher in infants with IVH compared to infants no-IVH developed (3.5 vs 1.7, respectively; p=0.018).
The rate of IVH and early mortality was 30.6%. Median (IQR) absolute NRBC count was 2.3 (1.6-19) /nL in infants with IVH and early mortality. It was found that absolute NRBC count were significantly higher in infants with IVH and early mortality (2.3 vs 1.4; p=0.003). The cut-off value for prediction of IVH and early mortality was NRBC >1.5 /nL with a sensitivity of 80% and a specificity of 50%.

Conclusions:
We conclude that a significant NRBC levels within the first 24 hours after birth might be a sensitive marker for an increased risk of IVH and early mortality. However, lower specificity of this marker should be kept in mind while predicting IVH and early mortality in VLBW infants.

NRBC, İntraventricular hemorrhage, Prematurity

ID 208 - A TWO-CENTER PREDICTIVE MODEL OF SEVERE INTRAVENTRICULAR HEMORRHAGE IN PRETERM INFANTS: PRELIMINARY RESULTS

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Background:
Severe intraventricular hemorrhage (IVH, grade 3-4) still remains a significant cause of mortality, morbidity and unfavorable neuro-developmental outcome in very preterm infants. Several pre- and post-natal parameters have been identified as risk-factors for its development. The aim of this study was to develop a predictive model of severe IVH in preterm infants using neonatal demographics and clinical characteristics (first 5 days of life).

Methods:
This is a retrospective study involving preterm neonates [≤ 32 weeks gestational age (GA)] admitted in two level III Neonatal Intensive Care Units during a 3-year time period (2017–2020). The study has a hierarchical two-level design: level 1 (neonates) and 2 (centers). Hypotheses of independence between the risk-factors in each center were explored with Log-Linear models. Two-level Generalized Mixed Linear Models to demonstrate the contribution of the significant risk-factors in the development of severe IVH. Accordingly, the optimal cut-off point was based on the calculated sensitivity and specificity following ROC analysis. All analyses were performed using the R statistical software.

Results:
232 neonates (129 and 103 from each center) participated in the study. The incidence of severe IVH in the two centers was 13.95% and 11.65%. Analysis of the significant risk-factors entered into the final model as dichotomous variables, revealed that the combinations of GA<28 weeks and patent ductus arteriosus as well as of cesarian section and birth weight ≤1000 g, intubation at birth, and male gender were significant predictors of severe IVH. The constructed model produced an AUC value of 0.872 (95%CI:0.811-0.934) while at the probability value 0.162, sensitivity and specificity were 83.33% and 82.18%, respectively.

Conclusion:
Several demographic and clinical characteristics could predict the probability of occurrence of severe IVH. Development of predictive models could help in early identification of preterm infants at increased risk of IVH allowing, thereby, the application of preventive measures as well as better parental counseling.
None

ID 262 - Assessment of pain and discomfort during less invasive surfactant administration (LISA) in preterm infants under non-pharmacological analgesia – preliminary results

Doctor Karin Pichler[1], Doctor Benjamin Kuehne[2], Professor Angelika Berger[1], Doctor Vito Giordano[1], Professor Angela Kribs[2], **Professor Katrin Klebermass-Schrehof[1]**

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Background and aims

The European Consensus Guidelines on the Management of RDS recommend LISA as the optimal method for surfactant administration. Still, there is no consensus on whether or not analgesia or sedation should be routinely used during LISA. This study aims to analyze if and to what extent pain and discomfort occur in preterm infants during LISA when non-pharmacological methods of analgesia are used.

Methods

Inborn preterm infants ≤34+0 weeks of gestation with RDS and the need for surfactant replacement were included in the study. LISA was performed as already published [Klebermass-Schrehof et al. 2013] and recorded on video. Standard non-pharmacological analgesia (oral succhrose, facilitated tucking) was used in all infants. Two independent observers assessed discomfort and pain before, during and after LISA using the COMFORTneo score and the Neonatal Pain, Agitation, and Sedation Scale (N-PASS).

Results

So far 17 infants have been included in the study with a mean gestational age of 28 weeks (+/- 3 weeks) and mean birth weight of 1156 g (+/- 466 g). All infants received LISA within 36 hours after birth. Before and after LISA the COMFORTneo score was <14 in all infants, which is considered acceptable comfort. During LISA 2 infants exceeded this threshold (maximum score 15 in one infant) (p=0.596). N-PASS did not exceed +3 in all infants at any time. This is considered as no signs of pain.

Conclusions

When non-pharmacological methods of analgesia were applied, 88% of infants were assessed as being comfortable and pain-free during LISA.

None declared

ID 521 - Melatonin increases NLRP3 inflammasome activation and serum IL-1ra concentration in neonatal encephalopathy

Doctor Tim Hurley[1,2,3], Doctor Lynne Kelly[1,2,3], Doctor Eman Isweisi[1,2,3], Professor Martin White[4], Professor Jan Miletin[4], Professor Afif EL-Khuffash[5], Professor Adrienne Foran[5], Professor Naomi McCallion[5], Doctor Claudine Vavasseur[6], Doctor Deirdre Sweetman[6], Professor Eleanor Molloy[1,2,3,4,7]

[1]Paediatrics and Child Health, Trinity College Dublin, Dublin, Ireland, [2]Trinity Translational Medicine Institute, Trinity College Dublin, Dublin, Ireland, [3]Trinity Research in Childhood Centre, Trinity College Dublin, Dublin, Ireland, [4]Department of Neonatology, Coombe Women and Infant's University Hospital, Dublin, Ireland, [5]Department of Neonatology, Rotunda Hospital, Dublin, Ireland, [6]Department of Neonatology, National Maternity Hospital, Dublin, Ireland, [7]Department of Neonatology, Children's Hospital Ireland at Crumlin and Tallaght, Dublin, Ireland

Background

Dysregulated inflammation is a key process in neuronal cell death in neonatal encephalopathy (NE). Activation of the NOD-, LRR- and pyrin domain-containing protein 3 (NLRP3) inflammasome results in increased transcription and cleavage of interleukin (IL)-1β and IL-18. Both are implicated in neuronal cell death in models of NE. IL-1ra, an anti-inflammatory cytokine, negatively regulates activation of the inflammasome. Early randomised trials in NE have shown improved outcomes with melatonin administration. One of the proposed anti-inflammatory effects of melatonin is inhibition of NLRP3 inflammasome activation.

Methods

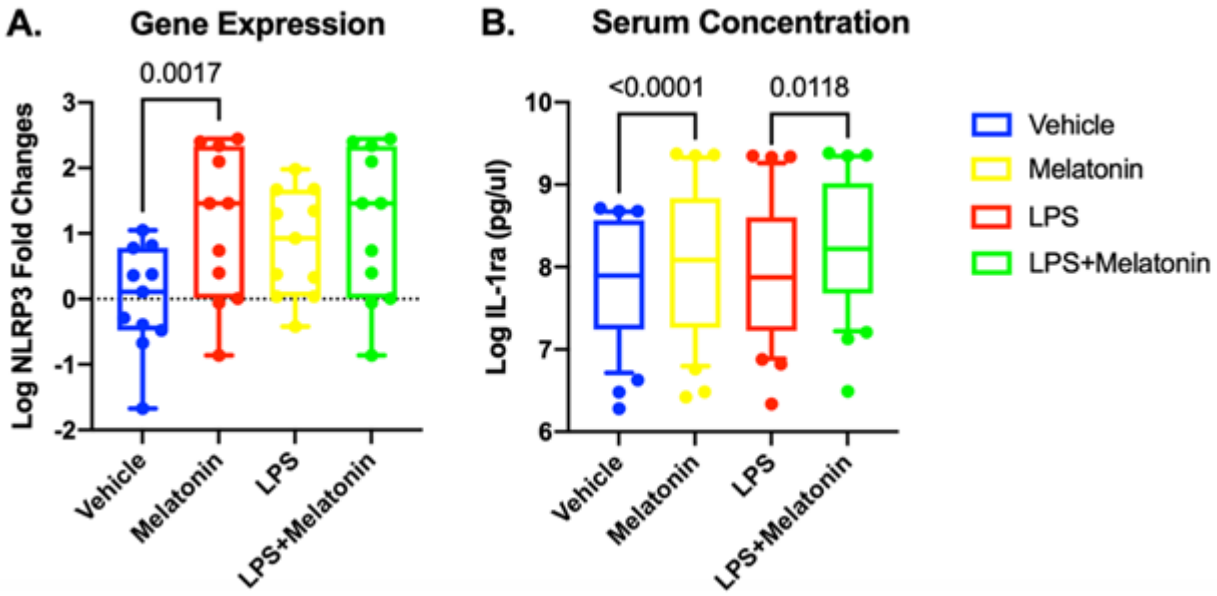
Whole blood samples were collected from infants with NE requiring therapeutic hypothermia (TH) during the first 5 days of life and divided into 4 treatment groups – vehicle, lipopolysaccharide (LPS), melatonin, and LPS + melatonin. Whole blood RNA was isolated, cDNA was synthesised and analysed by quantitative PCR for the expression of NLRP3, IL-1β, and apoptosis-related speck-like protein containing a caspase recruitment domain (ASC). Serum was analysed for IL-1β, IL-18, and IL-1ra cytokine concentration by multiplex ELISA. Differences between treatment groups in NLRP3 inflammasome genes and the correlation of gene expression with serum cytokines was examined by paired t-tests and Pearson correlation following data log transformation.

Results

Melatonin treatment resulted in a significant increase in NLRP3 expression compared to vehicle samples (n=36). No other differences between treatment groups in NLRP3, IL-1β, or ASC expression were observed when vehicle and melatonin groups or LPS treated and LPS+melatonin treated groups were compared. Melatonin treatment also resulted in a significant increase in serum IL-1ra concentration in compared to vehicle and LPS-stimulated samples. However, there were no significant changes in serum IL-1β or IL-18 concentration. In vehicle samples there was a significant association between NLRP3 expression and serum concentration of IL-1β.

Discussion

Melatonin treatment was associated with an increase in NLRP3 expression and IL1ra. Further exploration of the effects of melatonin on the inflammasome, associated cytokines, and immune cell functions are required. Melatonin has many other proposed mechanisms of action in NE, particularly antioxidant effects, and these also require exploration.



None declared

ID 538 - IMMUNOMOLDULATION WITH FINGOLIMOD IN NEONATAL HYPOXIC ISCHEMIA IN MICE

Doctor Isabella Schmeh[1,2], PhD Elena Di Martino[2,3], Prof. Ulrika Åden[1,2]

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Background

Timing of inflammatory processes is important for neurocognitive outcomes in neonatal hypoxic brain (HI) injury. Treatment with Fingolimod, a sphingosine-1-phosphate receptor agonist with T-cell modulating effects, has been shown to be beneficial in adult models of ischemia-induced neurodegeneration. On the other hand administration of Fingolimod directly after neonatal HI aggravated brain injury. We investigated the effects of a 3 weeks Fingolimod treatment starting 3 days after induction of neonatal hypoxic ischemia (HI) in mice.

Methods

We induced HI (n=37) in term-equivalent 10 days old C57BL/6 mice by electrocoagulation of the left common carotid artery followed by exposure to 10% oxygen/90% nitrogen for 60 minutes at 36°C +-1°C. The mice received treatment with 1mg/kg Fingolimod or vehicle (NaCl 0.9%) intraperitoneally 3, 10 and 17 days after HI. The control group of mice were sham operated (n=25). Behaviour testing comprised beam walking and Rotarod testing. The neuropathological score was assessed via Nissl stained cryoslices. By now, the Rotarod test results of 24 HI animals and 14 sham operated animals were available as well as neuropathological score and beamwalk results of 19 HI and 13 sham operated animals.

Results

The HI groups did not differ in body temperature and Fingolimod treatment did not affect weight gain. The Rotarod test results showed significant differences in motor skills between HI and sham groups (Fig. 1) but there was no significant difference between Fingolimod and vehicle treated groups. Morphological brain injury after HI was similar in the fingolimod and placebo groups.

Conclusion

Three weeks administration of Fingolimod starting 3 days after HI did neither improve nor exacerbate brain injury in our protocol. Further investigations are needed to evaluate a different time point of administration or dose may be beneficial.