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Section on Neonatal-Perinatal Medicine

ARTICLES OF INTEREST – July 2021

End-organ saturations correlate with aortic blood flow estimates by echocardiography in the extremely premature newborn – an observational cohort study
Gabriel Altit, Shazia Bhombal, Valerie Y Chock, et al. BMC Pediatr.

This is a single center study comparing echocardiography derived markers of ascending aorta (AscAo) and descending aorta (DesAo) blood flow with Near-infrared spectroscopy (NIRS) measures of cerebral saturation (Csat) and renal saturation (Rsat) obtained during the echo in extreme preterm infants <29 weeks gestation. The study included 49 neonates with 75 Csat-ECHO and 62 Rsat-ECHO observations (Mean PMA at echo 28.3 ± 3.8 weeks). Renal and cerebral fractional tissue oxygen extraction (rFTOE and cFTOE, respectively) were calculated. Preductal measures (AscAo velocity time integral (VTI) and AscAo output) correlated with Csat or cFTOE, while postductal measures (DesAo VTI, DesAo peak systolic velocity, and estimated DesAo output) more closely correlated with Rsat or rFTOE. The authors concluded that NIRS measures correlated with echocardiographic aortic blood flow measurements.

Methadone effectively attenuates acute and long-term consequences of neonatal repetitive procedural pain in a rat model
Nynke J van den Hoogen, Thomas J de Geus, Jacob Patijn, et al. Pediatr Res.

This study used methadone analgesia to prevent acute and long-term hypersensitivity associated with neonatal procedural pain in rat pups. Rat pups received either methadone (1 mg/kg) or saline prior to repetitive needle pricks into the left hind paw from postnatal day P0 to P7, while control littermates received a tactile stimulus. Mechanical sensitivity to Von Frey filaments was assessed during the neonatal period (P0-P7), from weaning to adulthood (3-7 weeks) and following surgical re-injury of the same dermatome in adulthood. The results showed that Methadone completely reversed acute hypersensitivity from P0 to P7. Long-term hypersensitivity was also prevented after re-injury in adulthood, without affecting sensitivity from weaning to adulthood.

Assessment of 2-year neurodevelopmental outcomes in extremely preterm infants receiving opioids and benzodiazepines
Mihai Puia-Dumitrescu, Bryan A Comstock, Sijia Li, et al. JAMA Netw Open.

Secondary analysis of the PENUT Trial sought to describe the association between opioid/benzodiazepine exposure and 2-year neurodevelopmental outcomes among infants born from 24 to 27 weeks at 19 US NICUs. Infants exposed to both opioids and benzodiazepines had adjusted OR of 9.7 for NEC and 1.7 for sBPD. They had a mean of 34 days longer hospital stay and had lower Bayley scores at 2 years of age. Prolonged exposure of any opioid or benzodiazepine (>7 days) was associated

with lower Bayley scores compared to non-exposed infants while short exposure (≤7 days) was not different. This study highlights variability in practice regarding the use of opioids and benzodiazepines in this population and questions the benefit of using these medications.

Hypotension in Preterm Infants (HIP) randomised trial
Eugene M Dempsey, Keith J Barrington, Neil Marlow, et al. Arch Dis Child Fetal Neonatal Ed.

10 NICUs across Europe and Canada participated in this RCT to study the early use of inotropes in hypotensive infants born <28 weeks. Patients with hypotension were treated with a 10mL/kg saline bolus followed by dopamine infusion or placebo; starting dose was 5mcg/kg/min and titration was allowed up to 20mcg/kg/min over 2 hours. Hypotension was defined as mean BP < gestational age for at least 15 minutes in the first 72 hours after birth. The primary outcome was survival to 36 weeks without ultrasound findings of severe brain injury. 58 patients were randomized with a mean gestational age of 25 weeks and mean birthweight ~700g. The dopamine group had fewer patients who required a second inotrope, but there were no differences in primary or secondary outcomes. The study was stopped early due to poor recruitment, and the authors conclude they did not detect any differences between the standard or restrictive approach to hypotension.

Safety and immunogenicity of a prototype recombinant alpha-like protein subunit vaccine (GBS-NN) against Group B Streptococcus in a randomised placebo-controlled double-blind phase 1 trial in healthy adult women
Per Fischer, Andrzej Pawlowski, Duojia Cao, et al. Vaccine.

Given that GBS is the leading cause of life-threatening infections in newborns, the authors sought to evaluate the safety and immunogenicity of a prototype vaccine consisting of the fused N-terminal domains of the AlphaC and Rib surface proteins of (GBS-NN). GBS-NN was well-tolerated and significantly increased antibody concentrations in healthy, non-pregnant women after two doses. The authors conclude that further testing and development of the vaccine are warranted.

Nasal high-frequency jet ventilation (NHFJV) as a novel means of respiratory support in extremely low birth weight infants
Jessica Keel, Theodore De Beritto, Rangasamy Ramanathan, et al. J Perinatol.

This retrospective study included 16 infants with BW <1000g who received Nasal High Frequency Jet Ventilation (NHFJV). Successful use was defined as avoiding intubation for at least 72 hrs after being placed on NHFJV. Median gestational age was 24.5 weeks (IQR 24, 25) and weight at the start of NHFJV was 1090g (IQR 905, 1250). NHFJV was used successfully in 13/16 (81%) infants with a mean duration of 7 days (IQR 3, 12).

Delivery room care and neonatal resuscitation while on intact placental circulation: an open-label, single-arm study
R UshaDevi, S Mangalabharathi, V Prakash, et al. J Perinatol.

This feasibility study evaluated 376 infants who received delivery room resuscitation with intact placental circulation (via trolley) at mother's bedside until 3 minutes after birth. Median gestational age was 38 (37-39) weeks and median birth weight was 2740 (2330-3120) grams. Of the 376 infants, 92 required resuscitation: 90 (97.8%) received PPV, 49 (53.2%) were intubated, and 13 (14.1%) received chest compressions.

Multisystem inflammatory syndrome in infants <12 months of age, United States, May 2020–January 2021
Shana Godfred-Cato, Clarisse A Tsang, Jennifer Giovanni, et al. Pediatr Infect Dis J.

The authors sought to describe the clinical course, laboratory findings, therapeutics and outcomes among infants diagnosed with multisystem inflammatory syndrome in children (MIS-C). Infants of age <12 months with MIS-C were identified by reports to the CDC's MIS-C national surveillance system. Eighty-five infants with MIS-C were identified and 83 (97.6%) tested positive for SARS-CoV-2 infection with a median age of 7.7 months. Rash, diarrhea, and vomiting were the most common signs and symptoms reported. Laboratory abnormalities included elevated C-reactive protein, ferritin, d-dimer, and fibrinogen. Infants appear to have a milder course of MIS-C than older children with resolution of their illness after hospital discharge. The full clinical picture of MIS-C across the pediatric age spectrum is evolving.

Association of preterm birth with long-term risk of heart failure into adulthood
Casey Crump, Alan Groves, Jan Sundquist, et al. JAMA Pediatr.

In this national cohort study conducted in Sweden including all singleton births during 1973-2014, the authors' objective was to determine whether preterm birth is associated with increased risk of heart failure (HF) from childhood into mid-adulthood. Out of 4 193 069 individuals included, 4158 persons (0.1%) were identified as having HF. Preterm birth (gestational age <37 weeks) was associated with increased risk of HF at ages < 1 year, 1-17 years, and 18-43 years compared with full-term birth (gestational age, 39-41 weeks). Between 18-43 years, HF incidence rates (per 100 000 person-years) were 31.7 for extremely preterm births (22-27 weeks), 13.8 for moderately preterm births (28-33 weeks), 8.7 for late preterm births (34-36 weeks), and 7.3 for early term births (37-38 weeks) compared with 6.6 for full-term births. The authors concluded that in this large national cohort, preterm birth was associated with increased risk of new-onset HF into adulthood and highlighted the need for long-term clinical follow-up into adulthood for risk reduction and monitoring for HF for survivors of preterm birth.

Outcomes of a uniformly active approach to infants born at 22–24 weeks of gestation
Fanny Söderström, Erik Normann, Maria Jonsson, et al. Arch Dis Child Fetal Neonatal Ed.

This was a single center retrospective cohort study to determine survival and outcomes in infants born at 22-24 weeks of gestation in a center with a uniformly active approach to management of extremely preterm infants born between 2006 and 2015. Short-term morbidities (such as retinopathy of prematurity, necrotizing enterocolitis, patent ductus arteriosus, intraventricular hemorrhage, peri-ventricular leucomalacia and bronchopulmonary dysplasia) and Neurodevelopmental outcomes (including incidence of cerebral palsy, visual impairment, hearing impairment and developmental delay) were assessed. Total survival was 64% (143/222), ranging from 52% at 22 weeks to 70% at 24 weeks. Of 133 (93%) children available for follow-up at 2.5 years corrected age, 34% had neurodevelopmental impairment with 11% classified as moderately to severely impaired. The authors conclude that a uniformly active approach to all extremely preterm infants results in more than 50% survival even in infants at 22 weeks with a majority being unimpaired at 2.5 years.

OTHER NOTEWORTHY PUBLICATIONS

COVID – 19

Multisystem inflammatory syndrome in infants <12 months of age, United States, May 2020–January 2021
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Correspondence: Vertical transmission of SARS-CoV-2 from infected pregnant mother to the neonate detected by cord blood real-time polymerase chain reaction (RT-PCR)

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https://pubmed.ncbi.nlm.nih.gov/33674714
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American Journal of Perinatology

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BASIC SCIENCE SELECTIONS
Acceleration of small intestine development and remodeling of the microbiome following hyaluronan 35 kda treatment in neonatal mice
Hala Chaaban, Kathryn Burge, Jeffrey Eckert, et al. *Nutrients.*

Altered hypothalamic DNA methylation and stress-induced hyperactivity following early life stress
Eamon Fitzgerald, Matthew C Sinton, Sara Wernig-Zorc, et al. *Epigenetics Chromatin.*

Insulin-like growth factor 1 in the preterm rabbit pup: characterization of cerebrovascular maturation following administration of recombinant human insulin-like growth factor 1/insulin-like growth factor 1-binding protein 3
Magnus Gram, Claes Ekström, Bo Holmqvist, et al. *Dev Neurosci.*

Serum glial fibrillary acidic protein as a biomarker of brain injury in premature neonates
Dimitra Metallinou, Grigorios Karampas, Georgia Nyktari, et al. *Bosn J Basic Med Sci.*

Thyroid hormones during the perinatal period are necessary to respiratory network development of newborn rats
Jean-Philippe Rousseau, Luana Tenorio-Lopes, Sergio Cortez Ghio, et al. *Exp Neurol.*

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Ya-Ting Su, Chun-Che Chiu, Shen-Hao Lai, et al. *Front Pediatr.*

Antibiotic-driven intestinal dysbiosis in pediatric short bowel syndrome is associated with persistently altered microbiome functions and gut-derived bloodstream infections
Robert Thänert, Anna Thänert, Jocelyn Ou, et al. *Gut Microbes.*

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Angelika Zankl, Jill Martin, Jane G Davey, et al. *Cochrane Database Syst Rev.*

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Tahereh Bahmani, Arezoo Karimi, Nazanin Rezaei, et al. *J Matern Fetal Neonatal Med.*

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Angela Dramowski, Sheylyn Pillay, Adrie Bekker, et al. *EClinicalMedicine.*