ARTICLES OF INTEREST – April, 2023

**Fewer glucose checks and decreased supplementation using dextrose gel for asymptomatic neonatal hypoglycemia**

This quality improvement program at a children’s hospital associated birth center evaluated the impact of a neonatal hypoglycemia clinical pathway implementing buccal dextrose gel use in late preterm (≥35 weeks) and term infants. Interventions included standardizing the clinical care for infants ≥35 weeks gestation who met criteria for asymptomatic hypoglycemia with the addition of dextrose gel as a primary treatment modality as well as an adjustment to the timing of post-intervention glucose checks. Over the 26-month period after QI implementation, 2703 infants were screened for hypoglycemia. Of these, 874 (32%) received at least one dose of dextrose gel. Use of dextrose gel was associated with lower number of mean glucose checks, lower use of supplemental milk and need for IV glucose.

**Respiratory outcomes for ventilator-dependent children with bronchopulmonary dysplasia**

This article describes the outpatient respiratory outcomes and center-level variability among children with severe bronchopulmonary dysplasia (BPD) who require tracheostomy and long-term mechanical ventilation. The data is from a retrospective cohort of subjects with severe BPD, born between 2016 and 2021, who received tracheostomy and were discharged on home ventilator support from 12 tertiary care centers participating in the BPD Collaborative Outpatient Registry. Notable findings among 155 patients who met inclusion criteria were the median age at time of tracheostomy placement 48 weeks’ postmenstrual age). The median ages of hospital discharge and first respiratory clinic visit were 10 months and 11 months of age, respectively. During the study period, 64% of the subjects were liberated from the ventilator at a median age of 27 months and 32% were decannulated at a median age of 49 months. There was remarkably wide variability across centers, the median ages for all key events differed significantly by center (P ≤ .001 for all events)

**Comparison and investigation of exosomes from human amniotic fluid stem cells and human breast milk in alleviating neonatal necrotizing enterocolitis**

The authors intend to compare the intervention effects of two types of exosomes on NEC mouse model and reveal their respective regulatory mechanisms. In general, both AFSC-derived exosomes (AFSC-exos) and HBM-derived exosomes (HBM- exos) can alleviate NEC- associated intestinal injury, significantly reduce NEC score, and reduce systemic and ileal inflammation and NEC related brain injury during experimental NEC. In vivo, the number of ileal crypts was more significantly restored after HBM-exos intervention than AFSC-exos, and in vitro, HBM-exos preferentially inhibited the inflammatory response
of intestinal epithelial cells (IECs), whereas AFSC-exos preferentially regulated the migration of IECs. Mechanistically, GO and KEGG analyses revealed the different therapeutic mechanisms of AFSC-exos and HBM-exos in NEC. Taken together, our results illustrate that AFSC-exos and HBM-exos reduce the severity of experimental NEC and intestinal damage through different mechanisms, supporting the potential of cell-free or breast milk free exosome therapy for NEC.

**Involvement of HIF1 stabilization and VEGF signaling modulated by Grx-1 in murine model of bronchopulmonary dysplasia**

Wenli Han, Fengmei Zhang, Dandan Mo, et al. *Cell Biol Int.*

The authors investigated whether the HIF-1alpha stabilization modulated by Grx1 ablation could ameliorate the pathological changes in the mouse model of BPD, including angiogenesis and alveolar formation. They found that depletion of Grx1 increased levels of GSH-protein adducts, which was associated with the improvement in the numbers of alveoli, the capillary density in the pulmonary microcirculation and the survival rate in the littermates with hyperoxic exposure. Grx1 ablation could promote HIF-1alpha glutathionylation by increasing GSH adducts to stabilize HIF-1alpha and to induce VEGF-A production in the lung tissue. These data indicate that HIF-1alpha stabilization plays a critical role in modification pulmonary microcirculatory perfusion, which is associated with the pathological damage under hyperoxic conditions, suggesting that targeting with HIF-1alpha stabilization should be a potential clinical and therapeutic strategy for BPD treatment.

**Three different regimens for vitamin K birth prophylaxis in infants born preterm: a randomized clinical trial**


This is a single center, open-label, parallel-group RCT studying the efficacy of 3 doses (1.0mg, 0.5mg, and 0.3mg, all IM) of vitamin K prophylaxis given at birth for preterm infants < 32 weeks and/or <1500g. Protein induced by vitamin K absence - II (PIVKA-II) levels were assessed at birth, and on days 5 and 28, along with mortality, bleeding manifestations, IVH, NEC, bilirubin levels, and duration of phototherapy. Both 1-mg and 0.5-mg IM vitamin K birth prophylaxis resulted in high sufficiency, compared with 0.3 mg. The current recommendation of 0.5-1 mg IM vitamin K should be continued for preterm infants.

**A network meta-analysis of intravenous versus oral acetaminophen for patent ductus arteriosus**


This is a meta-analysis comparing the efficacy of IV versus PO routes of acetaminophen administration on clinical outcomes related hsPDA in preterm neonates. Primary outcome assessed was rate of closure after the 1st and 2nd course. Secondary outcomes included NEC, mortality, BPD. Total of 21 RCTs were included in the analysis. Both PO and IV acetaminophen were efficacious in closing a PDA with oral ranking higher than IV (low confidence). Neither medication was better than no treatment for secondary outcomes of NEC or BPD (moderate and low confidence respectively).

**Maternal hypertensive disorders and survival without major morbidities among extremely low gestation newborns**


In this retrospective study the authors sought to evaluate if odds of survival without major morbidity are higher among extremely low gestation neonates (ELGANs) born to mothers with chronic hypertension (cHTN) or hypertensive disorders of pregnancy (HDP) compared to ELGANs born to mothers without hypertension (HTN). The primary outcome was survival to discharge without major morbidity. Multivariable regression models were used to compare outcomes among ELGANs born to women with cHTN, HDP, and no HTN. They found that after adjusting for contributing variables maternal HTN is not associated with improved survival free of morbidity among ELGANs.
Severity of small-for-gestational-age and morbidity and mortality among very preterm neonates

In this retrospective study the authors sought to evaluate the association between small for gestational age (SGA) severity and morbidity and mortality in a contemporary, population of very preterm infants. They analyzed neonatal outcomes in relation to weight for gestational age (WGA) and symmetry of growth restriction. An increase in WGA by one z-score was associated with decreased major morbidity or mortality risk (aRR 0.73, 95% CI 0.68-0.77) and other adverse outcomes. They found that increasing SGA severity had a significant impact on neonatal outcomes among very preterm infants.

Bivalent prefusion F vaccine in pregnancy to prevent RSV illness in infants

This phase 2b trial randomized pregnant women, at 24 through 36 weeks’ gestation, to receive either 120 or 240 μg of RSV prefusion F protein-based (RSVpreF) vaccine (with or without aluminum hydroxide) or placebo. In this planned interim analysis, 307 women received the vaccine. The geometric mean ratios of 50% neutralizing titers between the infants of vaccine recipients and those of placebo recipients ranged from 9.7 to 11.7 among those with RSV A neutralizing antibodies and from 13.6 to 16.8 among those with RSV B neutralizing antibodies. Transplacental neutralizing antibody transfer ratios ranged from 1.41 to 2.10 and were higher with nonaluminum formulations than with aluminum formulations. The authors concluded that RSVpreF vaccine elicited neutralizing antibody responses with efficient transplacental transfer and without evident safety concerns.

Cerebral oximetry monitoring in extremely preterm infants

This multicenter phase 3 trial randomized extremely preterm infants (gestational age, <28 weeks), within 6 hours after birth, to receive treatment guided by cerebral oximetry monitoring for the first 72 hours after birth or to receive usual care. A total of 1601 infants underwent randomization and 1579 (98.6%) were evaluated for the primary outcome of death or severe brain injury on cerebral ultrasonography at 36 weeks’ postmenstrual age. At 36 weeks’ postmenstrual age, death or severe brain injury had occurred in 272 of 772 infants (35.2%) in the cerebral oximetry group, as compared with 274 of 807 infants (34.0%) in the usual-care group (relative risk with cerebral oximetry, 1.03; 95% confidence interval, 0.90 to 1.18; P = 0.64). The incidence of serious adverse events did not differ between the two groups.

OTHER NOTEWORTHY PUBLICATIONS – April 2023

COVID-19
Gender analysis of Journal of Perinatology authorship during COVID-19
Clinical picture: Differential diagnosis of blue toes in a newborn baby: might have been maternal infection with COVID-19?
Incidence rates of medically attended COVID-19 in infants less than 6 months of age
SARS-CoV-2 during omicron variant predominance among infants born to people with SARS-CoV-2

Pediatrics
Early antibiotic use and neonatal outcomes among preterm infants without infections
Respiratory outcomes for ventilator-dependent children with bronchopulmonary dysplasia

Association of maternal BMI and rapid infant weight gain with childhood body size and composition

**Journal of Pediatrics**

Association of gestation and fetal growth restriction on cardiovascular health in preterm-born children

Betamethasone for preterm birth: auckland steroid trial full results and new insights 50 years on

Three different regimens for vitamin K birth prophylaxis in infants born preterm: a randomized clinical trial

Duration and consequences of periodic breathing in infants born preterm before and after hospital discharge

Changes in in-hospital survival and long-term neurodevelopmental outcomes of extremely preterm infants: a retrospective study of a japanese tertiary center

Transpyloric feeding is associated with improved oxygenation compared with gastric feeding among nonintubated extremely low birth weight infants

Preterm birth is associated with adverse cardiac remodeling and worse outcomes in patients with a functional single right ventricle

Hemodynamic characterization of neonates with congenital diaphragmatic hernia–associated pulmonary hypertension by cardiac catheterization

**Pediatric Research**

No new content

**Archives of Disease in Childhood - Fetal & Neonatal Edition**

No new content

**Journal of Perinatology**

Illuminating the path towards inclusivity: strategies to improve workforce diversity in neonatal-perinatal medicine

Monkeypox disease and pregnancy. Where are we today? A review of literature

Effect of maternal age on neonatal outcomes in very low birth weight singleton infants: a population-based study

Maternal hypertensive disorders and survival without major morbidities among extremely low gestation newborns

Severity of small-for-gestational-age and morbidity and mortality among very preterm neonates

Morbidity and mortality in neonates with Down Syndrome based on gestational age

Developing a resiliency model for survival without major morbidity in preterm infants

Parental ADHD and ASD symptoms and contributions of psychosocial risk to childhood ADHD and ASD symptoms in children born very preterm
Infantile hypertrophic pyloric stenosis: maternal diabetes and perinatal exposure to non-macrolide antibiotics

Antepartum periodontitis treatment and risk of offspring screening positive for autism spectrum disorder

Social disadvantage during pregnancy: effects on gestational age and birthweight

Levels of neonatal care among birth facilities in 20 states and other jurisdictions: CDC levels of care assessment toolSM (CDC LOCATeSM)

Neonatal intensive care unit occupancy rate and probability of discharge of very preterm infants

Neonatal mortality and disparities within the military health system

Implementing modified family integrated care in a U.S. neonatal intensive care unit: nursing perspectives and effects on parents

A biopsychosocial model of NICU family adjustment and child development

Time of birth and additional support need at school age: national cohort study of 865,409 children

Significant deficiency in mentorship amongst female neonatologists in the United States: a descriptive national survey by women in neonatology

Maternal and staff perceptions of shared reading in the neonatal intensive care unit

Fewer glucose checks and decreased supplementation using dextrose gel for asymptomatic neonatal hypoglycemia

A pivotal moment in the evolution of neonatal care

Recommendations to improve recruitment and retention of underrepresented in medicine trainees in neonatal-perinatal medicine

Increased risk of pulse oximeter bias in Black versus White preterm infants

Neonatology

American Journal of Perinatology

Evaluation of the neuroprotective effect of pycnogenol in a hypoxic–ischemic brain injury model in newborn rats

Neonatal outcome of babies born to women 40 years and older in a Jamaican birth cohort

Examining the validity of pediatric resident self-assessment in the delivery room

Differential alveolar and systemic oxygenation during preterm resuscitation with 100% oxygen during delayed cord clamping

Empirical antimicrobial therapy of neonates with necrotizing enterocolitis: a systematic review
What information do clinicians deem important for counseling parents facing extremely early deliveries? results from an online survey  

Does severity of brain injury on magnetic resonance imaging predict short-term outcome in neonates who received therapeutic hypothermia  

Factors that impact the timing and removal of gastrostomy placement/Nissen fundoplication in children with bronchopulmonary dysplasia  

Is lactoferrin supplementation beneficial for all preterm infants?  

Severity of maternal sars-cov-2 infection in pregnancy predicts neonatal outcomes  

**Journal of Neonatal-Perinatal Medicine**

No new content

**Maternal Health, Neonatology and Perinatology**

Benefits of maternally-administered infant massage for mothers of hospitalized preterm infants: a scoping review  

**Neoreviews**

Providing optimal nutrition to very low birthweight infants in the NICU  

Prenatal diagnosis, management, and treatment of fetal cardiac disease  

Does preterm status hinder the timely diagnosis of intestinal atresia?  

An infant with hypotonia and respiratory distress  

Newborn with a sudden increase in head circumference, wide sutures, and open fontanels  

Neonate with hypoglycemia and persistent jaundice  

A necessary iatrogenic preterm delivery: neonatal implications of antiphospholipid syndrome  

A term infant with respiratory distress after feeding  

A neonate with distinct eye movements  

**JAMA Pediatrics**

No new articles

**BMC Pediatrics**

Effect of eye shield and ear muffs on pain intensity during venous blood sampling in premature infants: a clinical trial study  

Maternal and umbilical cord blood lactate for predicting perinatal death: a secondary analysis of data from a randomized controlled trial  
**Pediatric Critical Care Medicine**
Single-center experience using the cardiohelp system for neonatal and pediatric extracorporeal membrane oxygenation
https://www.ncbi.nlm.nih.gov/pubmed/36571494

**New England Journal of Medicine**
Bivalent prefusion F vaccine in pregnancy to prevent RSV illness in infants
***Cerebral oximetry monitoring in extremely preterm infants
Azithromycin to prevent sepsis or death in women planning a vaginal birth
Commentary: Viral lineages in the 2022 RSV surge in the United States
Clinical images in medicine: Neonatal herpes simplex virus infection

**Lancet**
See COVID section

**JAMA**
Maternal opioid treatment after delivery poses low risk to infants
ADHD drugs in pregnancy not linked to children’s brain development
Majority of infant formula health claims are poorly supported

**BMJ**
No new articles

**Pediatric Infectious Disease Journal**
Safety and efficacy of ceftolozane/tazobactam versus meropenem in neonates and children with complicated urinary tract infection, including pyelonephritis: a phase 2, randomized clinical trial
Vaccine responses in congenital cytomegalovirus infection
Neonatal toxic shock syndrome-like exanthematous disease: a report of two cases
Meningitis among neonates with suspected sepsis presenting to pediatric emergency

**Pediatric Cardiology**
A network meta-analysis of intravenous versus oral acetaminophen for patent ductus arteriosus
Risk factors for tube feeding at discharge in infants undergoing neonatal surgery for congenital heart disease: a systematic review
Third trimester umbilical arterial pulsatility index is associated with neurodevelopmental outcomes at 2-years in major congenital heart disease
Assessing the risk of hypoglycemia secondary to propranolol therapy for the treatment of supraventricular tachycardia in infants
Relationship between human milk feeding patterns and growth in the first year of life in infants with congenital heart defects

Pediatric Neurology
Neurological and neuroradiological manifestations in neonates born to mothers with coronavirus disease 2019
Neurodevelopmental outcome at two years for preterm infants with intraventricular hemorrhage: a case-control study
Babies with pierre robin sequence: neuropsychomotor development

Obstetrics and Gynecology
Risk of stillbirth in pregnancies complicated by diabetes, stratified by fetal growth
Association between antenatal depression symptom trajectories and preterm birth
Deliveries among patients with maternal hepatitis C virus infection in the United States, 2000–2019

American Journal of Obstetrics & Gynecology
Risk of fetal or neonatal death or neonatal intensive care unit admission associated with gadolinium magnetic resonance imaging exposure during pregnancy.

Hospital Pediatrics
Improving the rate of delayed cord clamping in preterm infants: a quality improvement project
Limited utility of toxicology testing at delivery for perinatal cannabis use

BASIC SCIENCE SELECTIONS
Effects of cannabidiol, hypothermia, and their combination in newborn rats with hypoxic-ischemic encephalopathy
Global sphingosine-1-phosphate receptor 2 deficiency attenuates neuroinflammation and ischemic-reperfusion injury after neonatal stroke
Retinopathy of prematurity protection conferred by uteroplacental insufficiency through erythropoietin signaling in an experimental murine model
Involvement of HIF1 stabilization and VEGF signaling modulated by GRX-1 in murine model of bronchopulmonary dysplasia
Comparison and investigation of exosomes from human amniotic fluid stem cells and human breast milk in alleviating neonatal necrotizing enterocolitis
Dimethyl fumarate protects against intestine damage in necrotizing enterocolitis by inhibiting the toll-like receptor (TLR) inflammatory signaling pathway
Other noteworthy articles
Packed red blood cell transfusion as a predictor of moderate-severe bronchopulmonary dysplasia: a comparative cohort study of very preterm infants

Role of systemic inflammatory indices in the prediction of moderate to severe bronchopulmonary dysplasia in preterm infants

Comparison of post-treatment recurrence between ranibizumab injection and laser photocoagulation for type 1 retinopathy of prematurity

Biomarkers of hypoxic-ischemic encephalopathy: a systematic review

Empirical antimicrobial therapy of neonates with necrotizing enterocolitis: a systematic review

Screening inflammatory protein biomarkers on premature infants with necrotizing enterocolitis

Patent ductus arteriosus and development of bronchopulmonary dysplasia-associated pulmonary hypertension

Intermittent hypoxemia and bronchopulmonary dysplasia with pulmonary hypertension in preterm infants

Association of patent ductus arteriosus with extubation failure among preterm infants

Neurodevelopmental outcome at two years for preterm infants with intraventricular hemorrhage: a case-control study

Invasive fungal infection is associated with antibiotic exposure in preterm infants: a multi-centre prospective case-control study

Early laparoscopic-assisted surgery is associated with decreased post-operative inflammation and intestinal strictures in infants with necrotizing enterocolitis

Outcomes of combined endoscopic surgery and fibrinolytic treatment protocol for intraventricular hemorrhage: a randomized controlled trial

A network meta-analysis of intravenous versus oral acetaminophen for patent ductus arteriosus
Surgical ligation, not transcatheter closure, associated with a higher severity of bronchopulmonary dysplasia in extremely preterm infant intervened for patent ductus arteriosus