ARTICLES OF INTEREST – March, 2023

Ondansetron to reduce neonatal opioid withdrawal severity a randomized clinical trial

This multicenter, randomized, placebo controlled, double blind study randomized 90 patients to receive IV ondansetron or placebo in labor, followed by a daily infant dose of ondansetron or placebo for five days. Twenty-two (49%) ondansetron-treated and 26 (63%) placebo-treated infants required additional pharmacologic treatment (p > 0.05). In addition, Finnegan scores were lower in the ondansetron-treated group (4.6 vs. 5.6, p = 0.02) and there was a trend towards reduction in length of stay.

The effect of changing respiratory rate settings on CO2 levels during nasal intermittent positive pressure ventilation (NIPPV) in premature infants

This prospective, controlled, crossover study evaluated 50 premature infants (mean ± SD: 28.3 ± 2.4 weeks’ gestation) during two NIPPV rate changes, switching every hour between high (30 bpm) and low (10 bpm) breath states. The mean change in tcCO2 (95% confidence-interval), was -1.1 (-2.3 to 0.1) mmHg for increasing rate from low to high, and 0.46 (-0.49 to 1.41) mmHg for decreasing rate from high to low. The authors concluded that multiplying or dividing the rate settings by three did not significantly change the tcCO2 readings and that these findings could be helpful in the management of NIPPV ventilation settings for premature infants.

Clinical impact of less invasive surfactant administration using video laryngoscopy in extremely preterm infants

This is a single-center pre-post cohort study assessing clinical outcomes with the adaptation of less invasive surfactant administration (LISA) in extremely preterm infants. Primary outcome was need for invasive mechanical ventilation. Secondary outcomes were mortality, BPD, IVH ≥grade 3, and NEC. LISA was associated with reduced frequency of exposure to and duration of IMV in both ≤72 h after birth and during hospital stay and reduction in mortality, BPD, and IVH.

Inhaled nitric oxide in premature infants for preventing bronchopulmonary dysplasia: a meta-analysis
Yi Zheng, Qi Wu and Shuping Han. *BMC Pediatr.*

This is a meta-analysis of data assessed the effectiveness of inhaled nitric oxide (iNO) in reducing the risk of BPD in premature infants. 11 RCTs met screening criteria. The analysis showed that iNO group was associated with a significantly lower incidence of BPD than the control group (RR = 0.91, 95% CI 0.85-
there was significantly lower incidence of BPD with those treated with 10ppm. Also, the iNO group had an increased risk for NEC; however, no difference was seen in cases treated with 10ppm. No differences in the incidence of in-hospital mortality, IVH or PVL, and pulmonary hemorrhage.

The impact of maternal preeclampsia and hyperglycemia on the cardiovascular health of the offspring: a systematic review and meta-analysis

This systematic review assesses the impact of preeclampsia/eclampsia and/or gestational/pregestational diabetes mellitus on the health of the offspring (children <10 years of age). Across 45 studies and 2855 patients, health measures included anthropometry, cardiac dimensions and function, and vascular function were compared. The analysis demonstrated higher birth weight, systolic and diastolic blood pressure in the offspring of mothers with gestational diabetes compared to controls. In contrast, the offspring of mothers with preeclampsia had lower birth weight, however, they had increased systolic and diastolic BP compared to controls. These findings suggest that the in-utero milieu can have a permanent impact on the body composition and vascular health of the offspring.

Resuscitation with intact cord versus clamped cord in late preterm and term neonates: a randomized controlled trial

This open-label, randomized controlled trial was conducted in a tertiary care hospital in India. Neonates born at ≥34 weeks of gestation after a complicated pregnancy or labor were randomized just before birth to receive resuscitation according to the Neonatal Resuscitation Program algorithm with either an intact cord (intact cord resuscitation group) or after early cord clamping (early cord clamping resuscitation group). Intact cord group was resuscitated using a special resuscitation trolley on which the neonate could be received at the time of delivery and resuscitated while keeping the cord intact. The neonates randomized to the early cord clamping resuscitation group, the cord was clamped within 30 seconds of birth if the neonate was not breathing and resuscitation was initiated at the standard resuscitation corner. The primary outcome of the study was the expanded Apgar score at 5 minutes. The proportion of neonates who received PPV was lower in the intact cord resuscitation group (28.7% vs 36.5%, P = .05); Among neonates who received PPV, the expanded Apgar score at 5 minutes was significantly higher in the intact cord resuscitation group (median, 15 [IQR, 14-15] vs 14 [IQR, 13-15]; P < .001). The expanded Apgar score at 10 minutes, Apgar scores at 5 and 10 minutes, and oxygen saturation at 1, 5, and 10 minutes were also higher in the intact cord resuscitation group.

Randomized trial of surfactant therapy via laryngeal mask airway versus brief tracheal intubation in neonates born preterm

This was a randomized controlled trial including infants born at 27 to 36 weeks of gestation, >800 g, diagnosed with RDS and receiving fraction of inspired oxygen 0.30-0.60 via noninvasive respiratory support. Infants were randomized to surfactant via LMA (with atropine premedication) or ETT (InSuRE approach with atropine and remifentanil premedication). Surfactant therapy via LMA was noninferior to administration via ETT and it decreased early failures, possibly by avoiding adverse effects of premedication, laryngoscopy, and intubation.

Response categorization and outcomes in extremely premature infants born at 22–26 weeks gestation that received inhaled nitric oxide for hypoxic respiratory failure

Retrospective analysis of 107 infants born 22-26 weeks gestation who received iNO for hypoxic respiratory failure at a single institution. Infants were categorized as positive, negative, or no responders
based on change in FiO2 or OI. Underlying physiology was determined using Echocardiography/Radiography/Biochemistry. 63% of infants had a positive response; they received iNO earlier and were more likely to have acute pulmonary hypertension (PH). Positive response correlated with decreased incidence of death or grade 3 BPD at 36 weeks postmenstrual age, as compared to a negative response.

**Sepsis and mortality prediction in very low birth weight infants: analysis of HeRO and nSOFA**  

The heart rate characteristics (HRC) index (HeRO score) was developed as an early warning system for late-onset sepsis (LOS), and also rises before necrotizing enterocolitis (NEC). The neonatal sequential organ failure assessment (nSOFA) was developed to predict sepsis-associated mortality using respiratory, hemodynamic, and hematologic data. The aim of this study was to analyze the HRC index and nSOFA near blood cultures in VLBW infants relative to diagnosis and sepsis-associated mortality. In LOS/NEC, the HRC index increased before the blood culture, while nSOFA increased at the time of culture. Both scores were higher in nonsurvivors compared with survivors and in LOS/NEC compared with SRO. The nSOFA 12 hours after the time of blood culture predicted mortality during treatment better than any other time point analyzed (area under the curve 0.91).

**Prenatal and infant exposure to acid-suppressive medications and risk of allergic diseases in children**  

This nationwide, cohort study included data from South Korea’s National Health Insurance Service mother-child-linked database from January 1, 2007, to December 31, 2020. Participants included mother-child pairs of neonates born from April 1, 2008, to December 31, 2019. The findings of this cohort study suggest that there is no association between prenatal exposure to ASMs and allergic diseases in offspring. However, infant exposure to ASMs was associated with a higher risk of developing asthma, although the magnitude was more modest than previously reported.

**Sildenafil improves pulmonary vascular remodeling in a rat model of persistent pulmonary hypertension of the newborn**  

Persistent pulmonary hypertension of the newborn (PPHN) is characterized by pulmonary arterial remodeling mainly because of apoptosis resistance and excessive proliferation of pulmonary artery smooth muscle cells (PASMCs). Some reports have shown that sildenafil, a phosphodiesterase-5 inhibitor, exerts protective effects against PPHN, though the underlying molecular mechanism is not clear. These authors revealed that sildenafil effectively suppressed hypoxia-induced PASMC proliferation and apoptosis inhibition (P < 0.05). Sildenafil treatment significantly attenuated the induction of Notch3 and Hes1 induced by hypoxia treatment (P < 0.05). Furthermore, overexpression of Notch3 abolished the reduction of PASMC proliferation and promotion of PASMC apoptosis induced by sildenafil under hypoxia (P < 0.05). This study demonstrates that sildenafil shows a potential benefit against the development of PPHN by inhibiting Notch3 signaling, providing a strategy for treating PPHN in the future.

**OTHER NOTEWORTHY PUBLICATIONS – March, 2023**

**COVID-19**

Maternal, infant, and breast milk antibody response following COVID-19 infection in early versus late gestation  

SARS-CoV-2 placentitis, stillbirth, and maternal COVID-19 vaccination: clinical–pathologic correlations  
Effectiveness of BNT162b2 vaccination during pregnancy in preventing hospitalization for severe acute respiratory syndrome coronavirus 2 in infants

Pregnancy during a pandemic: a cohort study comparing adverse outcomes during and before the COVID-19 pandemic

**Pediatrics**

Pediatric ethics consultation services, scope, and staffing

Comparing strategies for critical congenital heart disease newborn screening

Pediatric ethics consultation services

Access to critical health information for children during emergencies: emergency information forms and beyond

Overuse of reflux medications in infants

Clinical pathways for the identification and referral for social needs: a systematic review

Pseudomonas meningitis and intracranial hemorrhage in IRAK-4 deficiency

**Journal of Pediatrics**

Randomized trial of surfactant therapy via laryngeal mask airway versus brief tracheal intubation in neonates born preterm

Delayed surgical closure of the patent ductus arteriosus: does the brain pay the price?

Provider perceptions on bereavement following newborn death: a qualitative study from Ethiopia and Ghana

Individual and family determinants for quality of life in parents of children with inborn errors of metabolism requiring a restricted diet: a multilevel analysis approach

Resuscitation with intact cord versus clamped cord in late preterm and term neonates: a randomized controlled trial

Acid suppression and antibiotics administered during infancy are associated with celiac disease

A secondary outcome analysis of a randomized trial using a mixed lipid emulsion containing fish oil in infants with extremely low birth weight: cognitive and behavioral outcome at preschool age

Bilirubin-displacing effect of ceftriaxone in infants with unconjugated hyperbilirubinemia born at term

Gastric pneumatosis in a neonate born late preterm on the first day of life

**Pediatric Research**

MicroRNA therapeutic targets in neonatal hypoxic–ischemic brain injury: a narrative review
Butyrate induces development-dependent necrotizing enterocolitis-like intestinal epithelial injury via necroptosis

Chemoprevention of bilirubin encephalopathy with a nanoceutical agent

Multiple exposures to sevoflurane across postnatal development may cause cognitive deficits in older age

Bacterial extracellular vesicles in the microbiome of first-pass meconium in newborn infants

Autonomic markers of extubation readiness in premature infants

Oxygen saturation histogram classification system to evaluate response to doxapram treatment in preterm infants

Characterization of lipoproteins and associated lipidome in very preterm infants: a pilot study

Effects of semi-upright swings on vital signs in NICU infants

Maternal acetaminophen use and cognitive development at 4 years: the Ontario Birth Study

Magnetic resonance venography to evaluate cerebral sinovenous thrombosis in infants receiving therapeutic hypothermia

Clinical impact of less invasive surfactant administration using video laryngoscopy in extremely preterm infants

Left ventricular diastolic function and respiratory outcomes in preterm infants: a retrospective study

Factors associated with MRI success in children cooled for neonatal encephalopathy and controls

Fathers’ sensitive parenting enhanced by prenatal video-feedback: a randomized controlled trial using ultrasound imaging

Body composition in term neonates of mothers with hypertensive disorders of pregnancy

Automated prediction of extubation success in extremely preterm infants: the APEX multicenter study

Preterm sepsis is associated with acute lung injury as measured by pulmonary severity score

Predictive value of the Thompson score for short-term adverse outcomes in neonatal encephalopathy

Maternal risk factors associated with offspring biliary atresia: population-based study

CpG methylation patterns in placenta and neonatal blood are differentially associated with neonatal inflammation

Late-onset neonatal sepsis: genetic differences by sex and involvement of the NOTCH pathway

Archives of Disease in Childhood - Fetal & Neonatal Edition
No new content
Impact of prenatal opioids on cardiac and autonomic development: systematic review and meta-analysis

Ondansetron to reduce neonatal opioid withdrawal severity a randomized clinical trial

Association of medication-assisted treatment and short acting opioids with newborn head circumference and birth weight

Association between pharmacologic treatment and hospital utilization at birth among neonatal opioid withdrawal syndrome mother-infant dyads

Accuracy of diagnostic codes for prenatal opioid exposure and neonatal opioid withdrawal syndrome

Capnography for catheter location confirmation in minimally invasive surfactant administration

The effect of changing respiratory rate settings on CO2 levels during nasal intermittent positive pressure ventilation (NIPPV) in premature infants

Nasal intermittent positive pressure ventilation as a rescue therapy after nasal continuous positive airway pressure failure in infants with respiratory distress syndrome

First week of life respiratory management and pulmonary ventilation/perfusion matching in infants with bronchopulmonary dysplasia: a retrospective observational study

Response categorization and outcomes in extremely premature infants born at 22–26 weeks gestation that received inhaled nitric oxide for hypoxic respiratory failure

Hyperinflation and its association with successful transition to home ventilator devices in infants with chronic respiratory failure and severe bronchopulmonary dysplasia

Neonatal respiratory support related to lung function abnormalities in school-age children with bronchopulmonary dysplasia

Racial differences in the impact of maternal smoking on sudden unexpected infant death

Sociodemographic factors and family use of remote infant viewing in neonatal intensive care

Beyond income: material hardship and the health and healthcare of premature children

Associations of household unmet basic needs and health outcomes among very low birth weight children

Racial and ethnic disparities in postnatal growth among very low birth weight infants in California

Prenatal care coordination, racial and socioeconomic inequities, and pre- and post-operative outcomes in hypoplastic left heart syndrome

European consensus guidelines on the management of respiratory distress syndrome: 2022 update

Agreement between noninvasive hemoglobin and laboratory hemoglobin measurements in neonates: a systematic review and meta-analysis
Early discontinuation of levothyroxine treatment is safe and feasible in extremely low birth weight infants with delayed hyperthyrotropinemia

Olfactomedin-4-positive neutrophils in neonates: link to systemic inflammation and bronchopulmonary dysplasia

Neonatal intensive care quality level-dependent variations in the survival rate of infants with a birth weight of 500 g or less in Korea: a nationwide cohort study

Transcatheter occlusion of left-to-right shunts in premature infants with bronchopulmonary dysplasia

The oxygen saturation index as early predictor of outcomes in congenital diaphragmatic hernia

Association between early feeding patterns and neonatal outcomes in very preterm infants: a retrospective cohort study

Oral ibuprofen is more effective than intravenous ibuprofen for closure of a patent ductus arteriosus: can pharmacokinetic modeling help us to understand why?

Mid-childhood outcomes after dextrose gel treatment of neonatal hypoglycaemia: follow-up of the sugar babies randomized trial

Incidence of intermittent hypoxemia increases during clinical care and parental touch in extremely preterm infants

Oxygen saturation ranges for healthy newborns within 2 h at altitudes between 847 and 4,360 m: a prospective cohort study

Placental transfusion strategies in preterm infants in low- and middle-income countries: a systematic review and network meta-analysis

Patterns of respiratory support by gestational age in very preterm infants

Magnetic resonance biomarkers and neurological outcome of infants with mild hypoxic-ischaemic encephalopathy who progress to moderate hypoxic-ischaemic encephalopathy

Assessment of change in practice of routine tracheal suctioning approach of non-vigorous infants born through meconium-stained amniotic fluid: a pragmatic systematic review and meta-analysis of evidence outside randomized trials

Validation of a new PCR-based screening method for prevention of Serratia marcescens outbreaks in the neonatal intensive care unit

Magnetic resonance imaging-based evaluation of anatomy and outcome prediction in infants with esophageal atresia

Discharge age and weight for very preterm infants in six countries: 2012–2020

Associations between early thyroid-stimulating hormone levels and morbidities in extremely preterm neonates

Brain biometry reveals impaired brain growth in preterm neonates with intraventricular hemorrhage
Predictive intelligent control of oxygenation in preterm infants: a two-center feasibility study

Enhanced parenteral nutrition is feasible and safe in very low birth weight preterm infants: a randomized trial

Transition of extremely preterm infants from birth to stable breathing: a secondary analysis of the CORSAD trial

Total fluid administration and weight loss during the first 2 weeks in infants randomized to early enteral feeding after extremely preterm birth

Recommendations for peripherally inserted central catheter insertion depths in neonates

**American Journal of Perinatology**

The impact of maternal preeclampsia and hyperglycemia on the cardiovascular health of the offspring: a systematic review and meta-analysis

Extended perinatal mortality audit in a rural hospital in India

Sepsis and mortality prediction in very low birth weight infants: analysis of HeRO and nSOFA

Analgesia, sedation, and neuromuscular blockade in infants with congenital diaphragmatic hernia

Parent perception of child safety following admission to a neonatal unit

Efficiency of lung ultrasonography in the diagnosis and follow-up of viral pneumonia in newborn

Immediate postnatal microbial colonization in sick term neonates admitted to NICU: prevalence, microbiota, and associated characteristics

**Journal of Neonatal-Perinatal Medicine**

No new content

**Maternal Health, Neonatology and Perinatology**

Association of maternal nationality with preterm birth and low birth weight rates: analysis of nationwide data in Japan from 2016 to 2020

Congenital pleuropulmonary blastoma in a newborn with a variant of uncertain significance in DICER1 evaluated by RNA-sequencing

**Neoreviews**

Collaboration between maternal-fetal medicine and neonatology when counseling at extreme prematurity

Diabetes mellitus in pregnancy

Small and mighty: micronutrients at the intersection of neonatal immunity and infection

Congenital cutaneous candidiasis in preterm infants
Umbilical cord bleeding in a neonate
(https://pubmed.ncbi.nlm.nih.gov/36854848/)

Dry gangrene of feet in an apparently well neonate

An infant with intrauterine growth restriction, a single umbilical artery, and abdominal wall defect
(https://pubmed.ncbi.nlm.nih.gov/36854849/)

Unilateral neck swelling in a newborn
(https://pubmed.ncbi.nlm.nih.gov/36854851/)

A neonate with obstructed nasal breathing
(https://pubmed.ncbi.nlm.nih.gov/36854852/)

Defining gender in infant care
(https://pubmed.ncbi.nlm.nih.gov/36854845/)

JAMA Pediatrics

Prenatal and infant exposure to acid-suppressive medications and risk of allergic diseases in children
(https://pubmed.ncbi.nlm.nih.gov/36622684/)

Association between neonatal intensive care unit type and quality of care in moderate and late preterm infants
(https://pubmed.ncbi.nlm.nih.gov/36648939/)

Associations between infant screen use, electroencephalography markers, and cognitive outcomes
(https://pubmed.ncbi.nlm.nih.gov/36716016/)

Mental health in infants and young children
(https://pubmed.ncbi.nlm.nih.gov/36716047/)

BMC Pediatrics

Effectiveness of antenatal dexamethasone in reducing respiratory distress syndrome and mortality in preterm neonates: a nested case control study
(https://pubmed.ncbi.nlm.nih.gov/36859189/)

Association between vitamin D level in mother’s serum and the level of vitamin D in the serum of preterm infants
(https://pubmed.ncbi.nlm.nih.gov/36859242/)

Parental experiences of live video streaming technology in neonatal care in England: a qualitative study
(https://pubmed.ncbi.nlm.nih.gov/36870975/)

Moral distress among neonatologists working in neonatal intensive care units in Greece: a qualitative study
(https://pubmed.ncbi.nlm.nih.gov/36890500/)

Premature infants receiving delayed cord clamping with and without cord milking: a randomized control trial
(https://pubmed.ncbi.nlm.nih.gov/36932370/)

Association between gestational weight gain and preterm birth and post-term birth: a longitudinal study from the national vital statistics system database
(https://pubmed.ncbi.nlm.nih.gov/36941673/)

Utilizing ultrasound in suspected necrotizing enterocolitis with equivocal radiographic findings
(https://pubmed.ncbi.nlm.nih.gov/36959616/)

Association between thiol-disulfide hemostasis and transient tachypnea of the newborn in late-preterm and term infants
(https://pubmed.ncbi.nlm.nih.gov/36966275/)

Analysis of risk factors associated with the high incidence of amblyopia in preterm infants at the corrected gestational age of 12 months
(https://pubmed.ncbi.nlm.nih.gov/36966278/)

Efficacy and safety of mucous fistula refeeding in preterm infants: an exploratory randomized controlled trial
(https://pubmed.ncbi.nlm.nih.gov/36854850/)
**Pediatric Critical Care Medicine**
Trends in neonatal extracorporeal membrane oxygenation during a venovenous cannula shortage

**New England Journal of Medicine**
No relevant articles

**Lancet**
No relevant articles

**JAMA**
Effect of intrapartum azithromycin vs placebo on neonatal sepsis and death a randomized clinical trial

**BMJ**
Maternal opioid treatment after delivery and risk of adverse infant outcomes: population based cohort study

**Pediatric Infectious Disease Journal**
Neonatal early-onset sepsis due to haemophilus influenzae in Utah

**Pediatric Cardiology**
Fetal diagnosis of scimitar syndrome in the presence of complex congenital heart disease
Changes in cerebral hemodynamics during systemic pulmonary shunt and pulmonary artery banding in infants with congenital heart disease
Reversal of fetal heart block in antibody-positive mother after hydroxychloroquine and dexamethasone
A case of neonatal lupus presenting with myocardial dysfunction in the absence of congenital heart block (CHB): clinical management and brief literature review of neonatal cardiac lupus

**Pediatric Neurology**
Neonatal human parechovirus encephalitis: a case of rapid and fatal gliosis
Pregnancy and child outcomes following fetal intracranial hemorrhage
A randomized comparative effectiveness study of reflexology, sucrose, and other treatments for needle procedures in newborns
BASIC SCIENCE SELECTION
Complex roles of TGF-beta signaling pathways in lung development and bronchopulmonary dysplasia
Causes of preterm birth: Genetic factors in preterm birth and preterm infant phenotypes
CpG methylation patterns in placenta and neonatal blood are differentially associated with neonatal inflammation
Sildenafil improves pulmonary vascular remodeling in a rat model of persistent pulmonary hypertension of the newborn
Apical-out enteroids as an innovative model for necrotizing enterocolitis
AMPK-driven macrophage responses are autophagy dependent in experimental bronchopulmonary dysplasia
Time-resolved transcriptomic profiling of the developing rabbit's lungs: impact of premature birth and implications for modelling bronchopulmonary dysplasia
Butyrate induces development-dependent necrotizing enterocolitis-like intestinal epithelial injury via necroptosis
SIRT3 improves alveolar epithelial cell damage caused by bronchopulmonary dysplasia through deacetylation of FOXO1

Other relevant articles
Outcomes of infants with severe bronchopulmonary dysplasia who received tracheostomy and home ventilation
Clinical impact of less invasive surfactant administration using video laryngoscopy in extremely preterm infants
Low dose paracetamol for management of patent ductus arteriosus in very preterm infants: a randomised non-inferiority trial
Associations between feeding and development in preterm infants in the NICU and throughout the first year of life
Routine contrast enema prior to stoma reversal seems only required following treatment for necrotizing enterocolitis: An evaluation of the diagnostic accuracy of the contrast enema

Association between endotypes of prematurity and pharmacological closure of patent ductus arteriosus: A systematic review and meta-analysis

NICU nurses' moral distress surrounding the deaths of infants

Utilizing ultrasound in suspected necrotizing enterocolitis with equivocal radiographic findings

Alpha/beta- and beta-blocker exposure in pregnancy and the risk of neonatal hypoglycemia and small for gestational age

Surfactant administration in preterm babies (28-36 weeks) with respiratory distress syndrome: LISA versus InSurE, an open-label randomized controlled trial

Systemic corticosteroid regimens for prevention of bronchopulmonary dysplasia in preterm infants

Physical compatibility of medications with concentrated neonatal and pediatric parenteral nutrition: A simulated Y-site drug compatibility study

Breast milk exposure is associated with cortical maturation in preterm infants