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Section on Neonatal-Perinatal Medicine

ARTICLES OF INTEREST – March 2022

Review: Red cell transfusion thresholds for preterm infants: finally, some answers
Edward F Bell. *Arch Dis Child Fetal Neonatal Ed.*

This article reviews the hemoglobin/ hematocrit thresholds used for red cell transfusion, focusing on two recent trials – ETTNO and TOP trials. This review reports that these trials found concordant and conclusive results without any difference in primary outcome, neurodevelopmental impairment at 2 years' corrected age or death before assessment within the range of hemoglobin transfusion thresholds studied. The review concludes that hemoglobin transfusion thresholds 11-13 g/dL for young critically ill or ventilated infants and 7-10 g/dL for stable infants not requiring significant respiratory support, can be safely used without expecting adverse consequences on survival or neurodevelopment.

Growth failure in infants with neonatal abstinence syndrome in the neonatal intensive care unit
Michael T Favara, Jessica Smith, Daniela Friedman, et al. *J Perinatol.*

This single-center retrospective study (2006-2018) investigated if infants with neonatal abstinence syndrome (NAS) are smaller at birth and have decreased growth parameters between birth and hospital discharge. Among 864 infants ≥35 weeks with NAS , the study showed that median percentiles were 30% (weight), 23% (HC) and length (37%), which decreased significantly ($p < 0.001$) at discharge to 12%, 6.5%, and 13%, respectively. The percentage of infants <3rd percentile increased significantly ($p < 0.001$) in all growth parameters from birth to discharge. The study concluded that NAS infants are smaller at birth and have significant postnatal growth retardation.

Zinc supplementation and the prevention and treatment of sepsis in young infants: a systematic review and meta-analysis
Omar Irfan, Robert E Black, Zohra S Lassi, et al. *Neonatology.*

A systematic review and meta-analysis looked at 11 randomized controlled trials involving 2,819 infants. Preventive studies suggested a protective effect of zinc supplementation on neonatal mortality rate (NMR) (risk ratio (RR) 0.28; 95% CI 0.12-0.67, LOW certainty), but with no effect on the incidence of sepsis, both in preterm neonates. Among young infants, therapeutic zinc was associated with significant reductions in infant mortality-rate (RR 0.61; 95% CI 0.41-0.93, LOW certainty) and treatment failure (RR 0.61; 95% CI 0.44-0.85; LOW certainty). Therapeutic zinc supplementation in neonates was associated with significant increase in serum zinc concentrations (mean difference 81.97; 95% CI 34.57-129.37; LOW certainty), but without an effect on hospital stay or NMR.

Reduction of severe intraventricular hemorrhage in preterm infants: a quality improvement project
Katelin P Kramer, Kacy Minot, Colleen Butler, et al. *Pediatrics.*

A multidisciplinary team aimed to reduce severe IVH by 50% within 3 years. Interventions included development of practice guidelines that focused on protecting the sensory environment, minimizing blood pressure lability, and encouraging parent engagement. Additional interventions included the use of early noninvasive ventilation, consistent use of antenatal betamethasone, and risk-stratified use of indomethacin for IVH prophylaxis. The study included 268 infants born <28 weeks or <1000g. They reduced serious IVH from 14% to 1.2% and reduced mortality by 50%. There were no increases in morbidities. The authors show that implementation of a multi-pronged neuroprotective strategy is associated with improved short-term outcomes.

Sixth-hour transcutaneous bilirubin and need for phototherapy in DAT positive newborns
Michael F Papacostas, Dwight M Robertson, Matthew D McLean, et al. *Pediatrics.*

This is a retrospective study of 346 newborns with ABO incompatibility who had both transcutaneous bilirubin and total serum bilirubin tests at 6 hours after birth. The objective was to determine the predictive ability of transcutaneous bilirubin among infants with ABO incompatibility. Transcutaneous bilirubin was found to be nearly as accurate as total serum bilirubin and reticulocyte count. Low (<3.0 mg/dL) and high (≥5.3 mg/dL) risk TcB cutoffs demonstrated a negative predictive value of 98% and positive predictive value of 85%, respectively. The authors conclude that current screening recommendations are not cost effective. A six-hour transcutaneous bilirubin is noninvasive, inexpensive, and reliably accurate to identify infants at high risk of phototherapy in the first 24 hours.

Umbilical cord milking in extremely preterm infants: a randomized controlled trial comparing cord milking with immediate cord clamping
Justin B Josephsen, Shannon Potter, Eric S Armbrecht, et al. *Am J Perinatol.*

This single-center randomized controlled trial included 56 infants between 24+0 to 27+6 weeks gestational age who were randomized to receive either umbilical cord milking (18 cm of cord milked three times) (UCM) or immediate cord clamping (ICC). There was no difference in the mean initial hemoglobin in the milking group compared with the ICC group, 13.7 ± 2.0 and 13.8 ± 2.6 g/dL, respectively ($p = 0.95$) and no difference in median number of blood transfusions after birth between the ICC and UCM groups, 2 (interquartile range [IQR]: 1-4) versus 2.5 (IQR: 1-5) ($p = 0.40$). There were also no differences in severe IVH, death, or neurodevelopmental outcomes at 15 to 18 months corrected gestational age.

Intrauterine inflammation exacerbates maladaptive remodeling of the immature myocardium after preterm birth in lambs
Amanda Vrselja, J Jane Pillow, Jonathan G Bensley, et al. *Pediatr Res.*

In preterm lambs, exposed antenatally to lipopolysaccharide, to mimic intra-uterine inflammation, there were distinct ventricular differences in cardiomyocyte growth and maturation trajectories as well as remodeling of the left ventricular myocardium compared to fetal controls observed. Antenatal exposure to lipopolysaccharide resulted in further collagen deposition in the left ventricle and a greater presence of immune cells in the preterm heart showing maladaptive cardiac remodeling and adversely impacts cardiomyocyte growth kinetics.

Pulmonary and neurologic effects of mesenchymal stromal cell extracellular vesicles in a multifactorial
Marissa A Lithopoulos, Lannae Strueby, Megan O'Reilly, et al. *Am J Respir Crit Care Med.*

In a multifactorial neonatal mouse model of lung injury and BPD, umbilical cord-mesenchymal stromal cell-derived extracellular vesicles, inserted intratracheally before ventilation, was shown to significantly

improve lung architecture, vessel formation, and inflammatory modulation. Additionally, it was shown to mitigate neuronal injury in the form of increased in vitro neurosphere formation and altered neural progenitor cell transcriptional signatures.

Italian neonatologists and SARS-CoV-2: lessons learned to face coming new waves
Maria Elena Cavicchiolo, Daniele Trevisanuto, Elena Priante, et al. *Pediatr Res.*

A joint European action plan is mandatory to face COVID-19 in neonates. This review summarizes available evidence from neonatal COVID-19 management in Italy. The current review can be useful in the management of the mother-neonate dyad during future waves of SARS-CoV-2

OTHER NOTEWORTHY PUBLICATIONS - March, 2022

COVID-19
Case report: neonatal cerebral venous thrombosis following maternal SARS-COV-2 infection in pregnancy
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The epidemiology of respiratory syncytial virus in New York City during the Coronavirus Disease-2019 pandemic compared with previous years
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https://pubmed.ncbi.nlm.nih.gov/35129576/
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https://www.bmj.com/content/bmj/376/bmj-2021-067696.full.pdf
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https://pubmed.ncbi.nlm.nih.gov/33790414/

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Review: Current evidence for prenatal and postnatal corticosteroids in preterm infants
https://pubmed.ncbi.nlm.nih.gov/33658282/

Review: Red cell transfusion thresholds for preterm infants: finally some answers
https://pubmed.ncbi.nlm.nih.gov/33906941/

Outcomes in relation to early parenteral nutrition use in preterm neonates born between 30 and 33 weeks' gestation: a propensity score matched observational study
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Hospital outcomes of infants with neonatal opioid withdrawal syndrome at a tertiary care hospital with high rates of concurrent nonopioid (polysubstance) exposure
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Providing support for neonatal intensive care unit health care professionals: a bereavement debriefing program
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Are early-onset sepsis evaluations and empiric antibiotics mandatory for all neonates admitted with respiratory distress?
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Antimicrobial susceptibility profiles among neonatal early-onset sepsis pathogens
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