

Theme: Neonatology

Paracetamol (acetaminophen) for patent ductus arteriosus in preterm or low birthweight infants (*Cochrane Database Syst Rev.* 2018;4:CD010061)

Use of intravenous or oral paracetamol is gradually becoming the preferred choice over ibuprofen or indomethacin for the management of hemodynamically-significant patent ductus arteriosus (hs-PDA). Safety, efficacy and previous reporting of prenatal or postnatal exposure to paracetamol and later development of autism or autism spectrum disorder remains the major concern. This updated Cochrane review included 916 infants (eight studies) to compare the use of paracetamol with other practices. GRADE analysis suggested that paracetamol is as effective as ibuprofen (moderate-quality evidence); more effective than placebo or no intervention (low-quality evidence); and as effective as indomethacin (low-quality evidence) in closing hs-PDA. No difference in neurodevelopmental outcome in children exposed to paracetamol, compared to ibuprofen was observed (low-quality evidence). Overall, serum creatinine levels, daily urine output and platelet counts were significantly better in the paracetamol group compared with indomethacin or ibuprofen group.

Efficacy of subthreshold newborn phototherapy during the birth hospitalization in preventing readmission for phototherapy (*JAMA Pediatr.* 2018;172:378-85)

Subthreshold phototherapy, defined as its initiation at total bilirubin below threshold levels, is often used in newborn infants to avoid subsequent re-hospitalization. This large retrospective study of a cohort of 25895 neonates born at 35 or more weeks' gestation documented that though subthreshold phototherapy reduced readmission rates, but the number needed to treat to avoid a single readmission ranged from 6 to 60, varying with the predicted risk of hyperbilirubinemia. The authors concluded that subthreshold phototherapy lengthened the newborn hospital stay, exposed the infant to the potential hazards of phototherapy including separation from its mother. In presence of good post-discharge follow-up services, it would be better to avoid subthreshold phototherapy during birth hospitalization.

Prolonged use of antibiotics after birth is associated with increased morbidity in preterm infants with negative cultures (*J Matern Fetal Neonatal Med.* 2018;23:1-201)

Preterm infants are often exposed to prolonged antibiotic therapy in spite of negative blood culture. Very few studies have been carried out to determine the beneficial and harmful effects of this practice. In this study, a cohort of 620 hospitalized infants of birthweight <1250 g with negative blood and CSF cultures in the first 2 days of life were followed up. Out of 620, 238 infants (38%) received initial empirical antibiotics greater than 5 days, whereas 382 (62%) received the same for up to 5 days. On multivariable regression analysis, the odds ratio (OR) for the

prolonged antibiotics group, adjusted for gestational age, SNAP II score, intra-uterine growth restriction, gender, maternal hypertension, prenatal steroid treatment, clinical chorioamnionitis, intrapartum antibiotic treatment, and multiple births, was 1.83 (1.15-2.92) for the composite outcome [necrotizing enterocolitis (NEC), late onset sepsis (LOS) and death], for LOS, 2.02 (1.20-3.39); and for bronchopulmonary dysplasia, 1.58 (1.04-2.29). Isolated mortality and NEC were not significantly different. The authors concluded that more than 5 days of antibiotic treatment in very preterm infants with negative cultures was associated with increased morbidity.

Neurobehavioral outcomes 11 years after neonatal caffeine therapy for apnea of prematurity (*Pediatrics.* 2018;141.pii:e20174047)

Caffeine is frequently administered to very low birth weight infants (VLBW) neonates to reduce the duration of respiratory support as for the management of apnea of prematurity. The study investigated the long-term neurobehavioral outcomes of the 11-year-old VLBW cohorts of the Caffeine for Apnea of Prematurity (CAP) trial. General intelligence, attention, executive function, visuomotor integration and perception, and behavior were assessed by regression models. The caffeine group performed better than the placebo group in fine motor coordination ($P=0.01$), visuomotor integration ($P<0.05$), visual perception ($P=0.02$), and visuospatial organization ($P=0.003$). General intelligence, attention, and behavior were similar, highlighting the long-term safety of caffeine therapy in VLBW neonates.

Rapid systematic review shows that using a high-flow nasal cannula is inferior to nasal continuous positive airway pressure as first-line support in preterm neonates (*Acta Paediatr.* 2018;doi: 10.1111/apa.14396)

Use of high-flow nasal cannula (HFNC), a respiratory support technique to provide heated and humidified mixture of oxygen and air through small nasal prongs at flow rates to match, or exceed, the patient's inspiratory flow rate, is growing popularity in NICUs due to its ease of application, reduced nasal trauma and perceived better comfort. There is a debate whether it is better than the age-old practice of nasal continuous positive airway pressure (nCPAP) as a first-line non-invasive respiratory support in preterm neonates. This systematic review analysed pooled results from 1227 neonates (six trials) and showed that HFNC was associated with a higher rate of failure than nCPAP in preterm neonates ≥ 28 weeks of gestation, with a risk ratio of 1.57 (moderate-quality evidence). No significant difference was observed between HFNC and nCPAP in the need for intubation and bronchopulmonary dysplasia rate (Low-quality evidence). However, rate of nasal injury was lower with HFNC (risk ratio 0.50).

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