Progeny HEALTH®

Best Practices

for Management of Infants with Apnea and Bradycardia of Prematurity

Definition

Apnea of prematurity (AOP) is commonly experienced by premature infants with an incidence inversely correlated with gestational age at birth. Nearly all babies less than 28 weeks of gestational age (GA) have this diagnosis, with 85% of those born at 30 weeks and 20% of those born at 34 weeks also experiencing AOP (Eichenwald 2016). Studies have shown that events may persist in many babies, at least until the completion of 43-44 weeks post-menstrual age (PMA). These events can persist despite an “apnea-free” period of observation while in the hospital prior to discharge.

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An apneic spell is usually defined as a cessation of breathing for 20 seconds or longer or a shorter pause accompanied by bradycardia (<100 beats per minute), cyanosis, or pallor. A clinically significant bradycardia is a heart rate less than 80 bpm for 5 seconds or more. (Patrinos 2020, Ahlfeld 2020, Eichenwald 2016, Guidelines for Perinatal Care 2017, Eichenwald 2017)

Underlyingconditions, such as sepsis or anemia, that may cause apnea should be considered and excluded prior to making the diagnosis of AOP. Infants born less than 35 weeks of gestation should be observed for clinically significant apnea and managed accordingly. In addition to chest wall impedance, heart rate and pulse oximeter monitoring should be performed on infants at risk for AOP.

Apnea of Infancy refers to infants greater than 37 weeks gestational age at the onset of apnea. These events typically are associated with other etiologies. (Benitz 2015)

Management

Prolonged or frequent events (defined as apnea >20 seconds and/or bradycardia with a heart rate 80 for at least 5 seconds) warrant evaluation to exclude underlying conditions and, if none are identified, treatment for AOP may be initiated. (Abdel-Hady 2015)

Pharmacologic measures such as methylxanthine therapy, particularly caffeine citrate, are often added to the treatment regimen if significant events persist. After the loading (20 mg/kg) and maintenance doses (5-10 mg/kg/day) of caffeine are ordered, additional boluses and maintenance dose adjustments may be required if apnea persists (Saroha 2020, Eichenwald 2016, Abdel-Hady 2015). Caffeine is the preferred prophylactic agent to prevent apnea of prematurity because of its longer half-life, wider margin of safety, and lower frequency of adverse effects when compared to theophylline (Henderson- Smart 2010). In addition to the benefit of acutely treating apnea of prematurity, long-term randomized-controlled Caffeine for Apnea of Prematurity (CAP) Trials have shown lower incidence of bronchopulmonary dysplasia (BPD), defined as oxygen treatment at 36 weeks postmenstrual age. In addition, there is long-term neuro- developmental safety and potential efficacy for reduced motor and visual impairments as late as 11 years of age. (Schmidt 2007, Schmidt 2012, Schmidt 2017, Mürner- Lavanchy 2018, Lodha 2019)

Non-pharmacologic measures, besides stimulation (Martin 2020, Cramer 2018), may include the application of air flow via nasal cannula and/or the addition of supplemental oxygen if hypoxemia exists. These measures may be useful in infants corrected to greater than 34 weeks GA, so discharge is not delayed awaiting caffeine clearance. Thermoregulation, infant positioning, and airway patency should be optimized.

Higher positive pressures (i.e., Nasal Continuous Positive Airway Pressure (NCPAP), High-flow nasal cannula (HFNC), Nasal Intermittent Positive Pressure Ventilation (NIPPV), or mechanical ventilation) may be indicated if events are severe and persistent and are not responding to other interventions (Firestone 2020). Red blood cell transfusions are sometimes prescribed in the presence of significant anemia with persistent and/or severe apnea, despite therapeutic caffeine levels.

A trial of discontinuation of caffeine should be considered at 33 weeks PMA or after a five-day period with minimal or no events (off positive pressure), whichever comes first(Eichenwald 2016). Routine monitoring of caffeine levels is not necessary since monitoring for clinical symptoms has been shown to be more effective (Eichenwald 2016).

Procedure or care related events, or events that occur during feeding, must be distinguished from AOP, and managed accordingly. Gastroesophageal reflux or suck/swallow incoordination are common conditions experienced by premature infants and are not associated with, nor contribute to, apnea of prematurity (Slocum 2009). Anti-reflux medications (i.e., antacids, prokinetic agents, proton-pump inhibitors) are not recommended in the neonate due to ineffectiveness and potential treatment complications of affecting the gastrointestinal tract adversely (Eichenwald 2016, Ho 2015, Tipnis 2009, Smith 2016).

An event-free period of up to 5 days for a preterm infant is a reasonable timeframe to demonstrate cardio-respiratory stability before safely discharging to home. (Coughlin 2020) The specific event-free period may need to be individualized for some infants depending on the gestational age at birth and the nature and severity of recorded events (Eichenwald 2016). Lorch et al. recognized that a longer countdown period (i.e., 7 days) may be appropriate for infants born at 26 weeks or less (Lorch 2011).

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Due to the long half-life of caffeine, the infant should continue to be monitored for five days after caffeine treatment has been discontinued (Chavez 2022, Dabin 2020, Darnall 1997) and for those born at 26 weeks gestational age or less, 7 days may be warranted.

Episodes of bradycardia that are brief and isolated or associated with oral feeding are common in preterm infants and are generally not considered significant (Patrinos 2020, Ahlfeld 2020).

A 5-day watch is not needed with feeding-related events Many experts do not count feeding-relating episodes in determining when to discharge these infant due to these types of events have a different pathophysiology than a true apnea/bradycardia event (Eichenwald 2016, Coughlin 2020, Slocum 2009). Oral feeding-related events should not preclude discharge (Coughlin 2020). Depending on the severity of the feeding-related event and the intensity of any possible intervention needed, consider a shorter observation period than 5 days.

Discharge Planning

The discharge of infants with a history of apnea can be challenging for the clinician, given the lack of clinical consensus. There may be variations in properly defining a true apnea, bradycardia, or desaturation event (Chandrasekharan 2020, Butler 2014, The Joint Commission Journal on Quality and Patient Safety 2016). There is also wide variation in the timing of caffeine discontinuation, despite recommendations from the Committee on Fetus and Newborn (2016), as mentioned above. Because caffeine has a long half-life, and to avoid unnecessary delays, it needs to be discontinued before the infant is ready to be discharged.

Monitoring clinical symptoms is more important than testing caffeine levels. It has been shown that monitoring of routine caffeine levels was not contributory to management (Eichenwald 2016), and it should not affect discharge. Research shows that caffeine has a half-life range of 62 to 112 hours in neonates (Doyle 2016). A 5-day observation time period is reasonable to demonstrate cardio-respiratory stability before a safe discharge from the hospital.

Pneumocardiograms (PCGs) are not recommended in identifying which neonates should be discharged with a home monitor. PCGs have a high false-positive rate and cannot accurately predict the occurrence of severe apnea or death (American Academy of Pediatrics Committee on Fetus and Newborn 2008). Since PCGs are not appropriate for routine screening, they are not an acceptable reason to delay discharge from the hospital (Ho 2015).

Infants who have been observed for an extended apnea-free or event-free period of time should be discharged without a monitor (Lorch 2011). The event-free period of time may vary based on the infant's gestational age at birth and characteristics of the recorded events. (Eichenwald 2016)

Home cardio-respiratory monitors may be used to facilitate the discharge of stable premature infants who manifest occasional mild or self-resolved "events," without cyanosis or respiratory distress. Infants requiring ongoing caffeine therapy may be considered for discharge with a monitor.

Events associated with feedings need not delay discharge

Home apnea monitors would also be appropriate for neonates who have respiratory technology-dependency (low-flow nasal cannula, ventilator, tracheostomy with collar, gastrostomy, etc.), unstable airways, rare medical conditions affecting regulation of breathing, or symptomatic chronic lung disease issues (Farrell 2002, Ramanathan 2001, Silvestri 2005, Zupanic 2003).

The American Academy of Pediatrics recommends against the use of commercial or store-bought high-tech baby monitors (Moon 2016). Parents should understand that the use of a home monitor has not been demonstrated to reduce the rate of SIDS, even in premature infants (Finer 2006, Ramanathan 2001, Moon 2016)

CPR training for parents and caregivers is highly recommended prior to discharge. Hospitals should ensure that training occurs in the facility, or that adequate instructional materials are provided, before discharging the infant.

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