Local Guideline

John Hunter Children's Hospital
CHILDREN, YOUNG PEOPLE AND FAMILIES

NSW GOVERNMENT Health
Hunter New England Local Health District

Apnoea and bradycardia management in NICU

Sites where Local Guideline applies	Neonatal Intensive Care Unit JHCH
Target audience:	NICU clinical staff, who provide care to neonatal patients.
Description	Guideline describing information about causes of apnoea and bradycardia to enable the best treatment and management for neonatal infants
This Local Guideline applies to:	
1. Adults	No
2. Children up to 16 years	No
3. Neonates – less than 29 days	Yes Approval gained from the Children Young People and Families Network on *9/12/14*
Keywords	Apnoea, Bradycardia, Caffeine, Desaturations, Preterm, Stimulation
Replaces Existing Local Guideline and Procedure	No
Registration Number(s) and/or name and of Superseded Documents	N/A

Related Legislation, Australian Standards, NSW Health Policy Directive, NSQHS Standard/EQuIP Criterion and/or other, HNE Health Documents, Professional Guidelines, Codes of Practice or Ethics:

- NSW Health Policy Directive 2007_079 Clinical Procedure Safety http://www0.health.nsw.gov.au/policies/pd/2014/pdf/PD2014_036.pdf
- NSW Health Policy PD 2005_406 Consent to Medical Treatment http://www.health.nsw.gov.au/policies/PD/2005/pdf/PD2005_406.pdf
- NSW Health Policy Directive PD 2007_036 Infection Control Policy http://www.health.nsw.gov.au/policies/pd/2007/pdf/PD2007_036.pdf
- NICU Clinical Practice Guideline 'Positioning for the sick or preterm neonate in NICU' JHCH_NICU_06.02 http://www.kaleidoscope.org.au/site/content.cfm?page_id=395217&current_category_code=8338&leca=930
- NSW Health Policy Directive PD 2012-062 Maternity-Safer Sleeping Practices for babies in NSW Public Health Organisations http://www0.health.nsw.gov.au/policies/pd/2012/pdf/PD2012_062.pdf

Prerequisites (if required)	N/A
Local Guideline Note	This document reflects what is currently regarded as safe and appropriate practice. The guideline section does not replace the need for the application of clinical judgment in respect to each individual patient but the procedure/s **require mandatory compliance**. If staff believes that the procedure/s should not apply in a particular clinical situation they must seek advice from their unit manager/delegate and document the variance in the patients' health record.
Position responsible for the Local Guideline and authorised by	Dr Paul Craven, Director of Newborn Services, JHCH
Contact Person	Jennifer Ormsby CNE(Relieving) NICU JHCH
Contact Details	Phone: 02 4985 5304 Email: Jennifer.Ormsby@hnehealth.nsw.gov.au
Date authorised	9/12/14

This Local Guideline contains advice on therapeutics	Yes Approval gained from Local Quality Use of Medicines Committee on *11/12/14*
Date of Issue	15/12/14
Review due date	15/12/18

Note: Over time links in this document may cease working. Where this occurs please source the document in the PPG Directory at: http://ppg.hne.health.nsw.gov.au/

RISK STATEMENT

This local guideline has been developed to provide guidance to clinical staff in NICU to assist in assessment and management of apnoea and bradycardia in the preterm infant. It ensures that the risks of harm to the infants whilst caring for an infant being assessed and managed for apnoea and bradycardia are identified and managed.

Any unplanned event resulting in, or with the potential for injury, damage or other loss to infants/staff/family as a result of this management must be reported through the Incident Information management System and managed in accordance with the Ministry of Health Policy Directive: Incident managaemtnPD2007_061. This would include unintended injury that results in disability, death or prolonged hospital stay.

RISK CATEGORY*:* *Clinical Care & Patient Safety*

OUTCOMES

1	To minimise the risk of impaired neurodevelopment by monitoring for episodes of bradycardia and apnoea
2	To treat apnoea and bradycardia before hypoxaemia occurs

ABBREVIATIONS & GLOSSARY

Abbreviation/Word	**Definition**
Postmenstrual age (PMA)	The time elapsed from the first day of the last menstrual period to birth (gestational age) plus the time elapsed after birth (chronological age).
Apneoa	A cessation of breathing for more than 20 seconds, or more than 10 seconds with associated bradycardia and /or oxygen desaturation / cyanosis (NIH consensus & NICHD Apnoea and Bradycardia Group 2006).
Desaturation	Desired oxygen saturation for a preterm infant admitted to NICU is between 90-94% (See pulse oximetry monitoring guideline, NICU document number 5.1.8)
Bradycardia	Heart rate less than 80 bpm for more than 10 seconds or if associated with color change, or >30 bpm change from resting heart rate.[2]
Apneoa of prematurity	Clinically significant apnea in a premature infant (less than 37 weeks gestation). Apnoea and bradycardia is a diagnosis of exclusion as there are many other causes of pathological apnea in a premature infant

BPD	Bronchopulmonary Dysplasia (Chronic lung Disease)
CAP trial	**Caffeine for Apnea of Prematurity (CAP)** is an international, multi-centre, randomized controlled trial to determine whether survival without neurodevelopmental disability at a corrected age of 18 months is improved if apnea of prematurity is managed without Caffeine in infants weighing 500 -1250 grams at birth
CO_2	Carbon dioxide
CPAP/NIPPV	Continuous Positive Airway Pressure/ Non -invasive positive pressure ventilation
PDA	Patent Ductus Arteriosis

Guideline Title - One Page Summary and Checklist

(Ctrl+Click on **Coloured** words to jump to that section)

This guideline is intended to assist clinical decision making for individual patients, not replace it. It will not apply equally to all infants, despite similar diagnoses.

Rationale: Top

To provide guidelines for management of Apnea and Bradycardia of Prematurity in infants less than 44 weeks postmenstrual age admitted to the neonatal unit of John Hunter Children's Hospital.

Background Top

Brief pauses in breathing (five to ten seconds) are common, particularly in preterm infants, and when they alternate regularly with breathing efforts, this is called periodic breathing. In some infants the pauses are prolonged and rapid depletion of oxygen stores leads to hypoxaemia and reflex bradycardia.

Incidence of Apnoea and Bradycardia Top

The incidence of apnoea in premature neonates is inversely correlated with gestational age at birth and birth weight. [3]

- 7 % at 34 to 35 weeks
- 15% at 32 to 33 weeks
- 54% at 30 to 31 weeks
- Nearly all infants born at less than 29 weeks /1,000 g

Types of Apnoea and Bradycardia Top

Apnoea and bradycardia is subdivided in three types and in each individual infant, one type may predominate

- **Central (10 to 25%) :** Cessation of both airflow and respiratory effort
- **Obstructive (10 to 25%):** Cessation of airflow in the presence of continued respiratory effort**.**
- **Mixed (50 to 75%):** Apnoea contains elements of both central and obstructive apnoea, either within the same apnoeic pause or at different times

Diagnosis of Apnoea and Bradycardia Top

Apnoea and bradycardia is a clinical diagnosis. All sick neonates and all neonates less than 35 weeks PMA admitted to the neonatal unit are monitored to detect significant cardio-respiratory events that may warrant clinical attention.

Conditions causing or accentuating apnoea

Top

Infection (bacterial and viral)	Sepsis, meningitis, NEC
Neurological	Intracranial haemorrhage
	Seizures
	Asphyxia
	Congenital malformations
Respiratory/Cardiovascular	Hypoxaemia, RDS, pneumonia
	aspiration
	PDA
	Hypovolaemia, hypotension
	Heart failure
Haematological	Anaemia
Gastrointestinal	GORD
	Abdominal distension
Drugs (infant and maternal)	Opiates
	Magnesium
	Prostaglandins
	Consider drug withdrawal
Acute/chronic pain	
Airway malformation	
Head/body position	
Metabolic	Hypoglycaemia
	Hypocalcaemia
	Hypothyroidism
	Hyponatraemia

Ref: Atkinson & Fenton. (2009) [28]

Consequences of Apnoea and Bradycardia

Top

- Prolonged hypoxaemia and reflex bradycardia which may require active resuscitation
- Frequent and prolonged episodes might be harmful to the developing brain. In contrast to earlier studies [5], recent studies show impaired neurodevelopment associated with prolonged, frequent episodes of apnoea and bradycardia especially if apnoea and bradycardia persists beyond 34 weeks post menstrual age (PMA). [6,7]
- Apnoea and bradycardia is not an independent risk factor for sudden infant death syndrome (SIDS). [8]

Interventions for Apnoea and Bradycardia

Top

Interventions for apnoea and bradycardia include efforts to keep airway open, reduce work of breathing and increase respiratory drive. If the background oxygen saturation in between apnoeic events is low (less than 90%) a small increment in the supplemental oxygen may also help reduce the severity and frequency of apnoea and bradycardia.

Positioning

Prone positioning can improve thoraco-abdominal synchrony, stabilize the chest wall and reduce apnoea and bradycardia.[9] Head elevated tilt position and three-stair-position do not offer any added advantage over standard prone position.[9]

It is widely accepted that sleeping a baby on its back at home reduces the risk of sudden infant death syndrome. However, whilst a preterm infant is continuously monitored in the NICU, it is safe to nurse the infant in side-lying or prone position. (See CPG 'Positioning preterm or sick neonate in NICU', JHCH_NICU_6.02).

Tactile stimulation

Tactile stimulation such as moderately stroking infant's leg is the most common intervention in response to apnoea and bradycardia. This intervention most likely works by generating excitatory, nonspecific neuronal activity in the brainstem centre to stimulate respiratory activity.[10]

Kangaroo care

Kangaroo care has achieved widespread acceptance for stable infants because of the calming effects on the baby's clinical status and vital signs. A randomized controlled trial showed that infants receiving kangaroo care had fewer apneic and bradycardic events than those who did not receive kangaroo care.[11.] Refer to CPG for more details 'Kangaroo care in NICU' JHCH_NICU_06.04

Kinesthetic Stimulation

Systematic review has shown that kinesthetic stimulation such as vigorously oscillating mattress is not effective in preventing apnoea and bradycardia.[12]

Nasogastric Vs Oro-gastric tube

Nasogastric tubes have been shown to increase nasal airway resistance by 50%. Therefore, oro-gastric feeding tubes are sometimes preferred in premature infants with apneic events. However, a recent randomized controlled trial showed that the placement of the feeding tube had no significant effect on bradycardia and desaturation.[13]

Olfactory stimulation

Pleasant odours increase respiratory drive, whereas unpleasant odours cause decreased respiratory effort, during active sleep when apnea is more common.

Marlier et al showed that exposure of preterm infants to Vanillin significantly reduced episodes of apnea. However, duration of this beneficial effect is not known as infants were studied for a short duration of 24 hours .[14]

CO_2 inhalation

CO_2 is the physiologic stimulus for breathing. Recently, a randomized controlled trial of theophylline versus CO_2 inhalation for treating apnoea and bradycardia showed that inhalation of a low CO_2 concentration (0.8%) in premature infants is as effective as theophylline in decreasing apnea without effecting cerebral blood flow velocity.[15] However, it is likely that infants will quickly accommodate to an inspiratory CO_2 concentration, and the effectiveness of long-term exposure is not known.

Red Blood Cell Transfusion

Data on the effect of blood transfusion on apnoea and bradycardia is not clear. A systematic review of liberal versus restrictive threshold of blood transfusion showed no benefit of transfusion on reduction in incidence of apnoea in either mildly or severely anaemic infants[16]. A recent randomized trial in premature infants comparing liberal with restrictive transfusion protocols found that infants in the restrictive transfusion group had a higher incidence of apnea[17].

CPAP and NIPPV

CPAP can enhance functional residual capacity and reduce the work of breathing; improving oxygenation and decreasing bradycardia (see 'CPAP in NICU' JHCH NICU_12.02. CPAP works effectively to reduce the incidence of obstruction, but it has no clear role in prevention of central apnoea and bradycardia[18]. A systematic meta-analysis has shown NIPPV to be effective for the treatment of apnoea and bradycardia[19.] In other words, reduced work of breathing may be the key to improving apnoea and bradycardia, which can be achieved via either synchronized NIPPV or variable flow NCPAP devices.

Pharmacological Management

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Methylxanthines

Both Theophylline and Caffeine are powerful central nervous system stimulants. They are non-selective antagonists of adenosine receptors. They increase ventilation, CO_2 sensitivity, and respiratory drive and decrease the hypoxic depression of breathing and improve diaphragmatic and respiratory muscle function. Caffeine is the preferred treatment for apnoea and bradycardia as it is just as effective as theophylline and has higher therapeutic ratio with less side effects, more reliable enteral absorption and a three-times longer half-life which allows for once daily administration.

When to start treatment

Top

Prophylactic

The CAP trial subgroup analysis showed that preterm infants <1250gm at birth who received prophylactic caffeine had lower odds (OR=0.74) of developing BPD compared to the placebo group[21]. A recent systematic review by Henderson-Smart showed that prophylactic caffeine administration significantly reduces the need for surgical ligation of PDA in preterm infants[20]. Hence, at NICU, JHCH, we recommend prophylactic caffeine for all infants < 29 weeks GA or weight < 1250g at birth.

Treatment

Infants >29 weeks GA or BW > 1250 should receive caffeine if they develop 2 or more episodes of apnoea and bradycardia requiring intervention.

Dosing Schedule
A loading dose of 20 mg/kg of Caffeine Citrate (oral - 10mg/kg of Caffeine Base) and maintenance dose of 10 mg/kg of Caffeine Citrate (oral - 5mg/kg of Caffeine Base) is effective and safe in the management of apnoea and bradycardia.[23, 24]

NB. 2mg caffeine citrate = 1mg caffeine base

Steer et al. compared a high loading dose of 80 mg/kg followed by 20 mg/kg of caffeine citrate every 24h with a standard loading dose of 20 mg/kg followed by 10mg/kg every 24h. The high-dose group showed significant reductions in re-intubation rate in 7 days post extubation without any long term side effects. [25]

When to cease treatment
There are no trial data to support decisions about when to cease treatment. However, lower the gestational age at birth, the longer the period that apnoea and bradycardia persists. Most infants are free of major apnea and bradycardia events by 36 to 40 weeks PMA[26]. Extremely premature infants may not achieve this control until 43-44 weeks PMA[27]. Infants who develop moderate to severe chronic lung disease may also achieve this milestone at a later age compared to infants without BPD.

Well infants who have been free of apnea/bradycardia event for at least 5 days and requiring no or minimal respiratory support may be trialed off caffeine at 33 weeks PMA.

In infants with moderate to severe chronic lung disease, overall physiological maturity should also be considered and decision to stop caffeine should always be discussed with the Neonatologist in charge.

Adverse Events

Top

Caffeine has a wide therapeutic index and levels need not be checked routinely.[22] Measuring drug levels should only be considered if toxicity or suboptimal dosing is clinically suspected.

Serum caffeine levels

- **Between 102-205 micromol/L are therapeutic**
- **> 250 micromol/ml may cause**
  Irritability, jitteriness, feeding intolerance and tachycardia, tachypnoea, vomiting, hypertonia, cardiac arrhythmia and seizures.

Doxapram

Doxapram is as effective as Methylxanthines in prevention of apnoea of prematurity. However there are concerns about the side effects of Doxapram such as, hypertension, QTc prolongation, seizures, vomiting, diarrhoea, and urinary retention and there are no long term data on this drug.

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AUTHOR: Nilkant Phad, Neonatal Fellow, NICU JHCH

REVIEWERS: Paul Craven, Neonatologist, NICU JHCH
Javeed Travadi, Neonatologist, NICU JHCH
Anil Lakkundi, Neonatologist, NICU JHCH
Julie Gregory, CNE, NICU JHCH
Denise Kinross CNC Newborn Services JHCH
Michelle Jenkins Senior Pharmacist JHCH
Vivienne Whitehead CNE NICU JHCH

APPROVED: NICU Executive Management Committee 5/11/14

FEEDBACK

Any feedback on this document should be sent to the Contact Officer listed on the front page.