Management of apnoea on the neonatal unit
Full Clinical Guideline

Reference no.: NIC RC02 NICU

Introduction
Apnoea is defined as cessation of breathing for more than 20 seconds. It is frequently associated with bradycardia and hypoxemia (fall in oxygen saturation).

In infants of any gestational age, frequent episodes of apnoea may indicate an underlying illness such as an infection. Infants must be appropriately assessed to ensure that any underlying pathology is investigated and treated, if required.

Apnoea of prematurity is the occurrence of frequent apnoeic episodes, often with bradycardia and desaturations, in infants born at <34 weeks gestational age. It is almost universal among extremely premature infants. It occurs due to the immaturityof the central respiratory control systems.

1 Aim and Purpose

a. Diagnosis, investigations, and management of apnoea in newborn infants

b. Use of caffeine for management of apnoea of prematurity

c. Guidance for heart rate and oxygen saturation monitoring for apnoea, bradycardia,and oxygen desaturations

2 Definitions, Keywords

Apnoea: cessation in breathing lasting for more than 20 seconds

Bradycardia: fall in heart rate to less than 90 beats per minute

Desaturation: fall in oxygen saturation level below the target range of 91-95% or as appropriate for corrected gestational age.

3 Introduction

Infants who have frequent episodes of apnoea, especially with with bradycardia and/or desaturations, and/or need physical stimulation or positive pressure ventilation, must be assessed to consider conditions such as:

- An inter-current respiratory illness such as lung infection or atelectasis
- Sepsis
- Necrotising enterocolitis
- Metabolic disturbances including hypoglycaemia
- Underlying neurological disorder such as causes of central hypotonia, or loss ofrespiratory drive
- Neonatal encephalopathy (HIE, meningitis, intracranial haemorrhage, seizures)
- Anaemia
- Gastro-oesophageal reflux disease

In the absence of suspicion of such pathological conditions, preterm infants who have apnoea should be considered to have apnoea of prematurity.

3.1 Treatment of apnoea of prematurity

Caffeine is used to treat apnoea of prematurity. It reduces thefrequency of apnoea, intermittent hypoxemia, and risk of chronic lung disease.

Caffeine therapy in preterm infants may improve long term outcomes: infants who received caffeine in a large randomised controlled trial (the Caffeine for Prematurity (CAP) trial) had higher rates of survival without neurodisability at 18-21 months of age[1]. Although there was no difference at 5 years of age [2], follow up at 11 years of age found significantly reduced motor impairment among those who had been treated with caffeine . Caffeine also reduced the risk of extubation failure in very preterm infants [4].Caffeine is easy to administer, cost effective, and well tolerated by infants.

Potential adverse effects of caffeine include tachycardia, increase urinary sodium loss, glucose intolerance, and jitteriness. However, in practice, these are very rare at the usual doses of caffeine used in newborn infants. Caffeine, especially at high does, may worsen gastro-oesophageal reflux disease.

3.2 Indication for caffeine therapy

- Infants born at <32 weeks gestational age
- Infants born at <34 weeks gestational age requiring mechanical ventilation (prior toplanned extubation)
- Any infant suspected to have apnoea of prematurity

3.3 Treatment regimen

3.3.1 Route of administration

Oral or intravenous (IV); oral route is preferred if infant on enteral feeds (when receiving at least 50% of total feed requirement).

3.4 Time of starting caffeine therapy

Caffeine should be started early (as soon after birth as possible) in infants who are

- <32 weeks' gestational age and breathing spontaneously or on non-invasive respiratory support
- <34 weeks' gestational age and on non-invasive respiratory support

The Perinatal Excellence to Reduce Injury in Preterm Birth (PERIprem) initiative suggests that the loading dose of caffeine should be started in all infants born at <30 weeks' gestation or <1.5 kg birth weight within 6 hours of birth.

In infants 30-34 weeks' gestational age infants who require mechanical ventilation after birth, caffeine may be started early or before a planned extubation.

3.4.1 Loading dose

20 mg/kg caffeine citrate once

3.4.2 Maintenance dose

5 mg/kg caffeine citrate once daily starting 24 hours after the loading dose.

Can beincreased to 10 mg/kg once daily if required.

Higher loading doses (>20mg/kg or higher maintenance does >10 mg/kg/d) have little or no effect in improving outcomes and may be harmful, especially in the extremely preterm infants who have high risk of intracranial bleeding [6].

3.4.3 Duration of caffeine therapy

Caffeine can be stopped in infants who are ≥34 weeks postmenstrual age and are no longer having apnoea or need respiratory support.

It may be continued in babies who require respiratory support for longer.

Caffeine has a long half-life and can be abruptly stopped but should be stopped at least 2 days before discharge home.

3.4.4 Monitoring caffeine levels

Caffeine levels are not monitored routinely. Only measure plasma concentrations of caffeine if inadequate clinical response, desired range 10-20mg/l (50-100 micromol/l) (see British National Formulary –children for furtherguidance)

3.4.5 Heart rate and oxygen saturation monitoring

Infants on caffeine should be monitored with continuous heart rate and oxygen saturation monitoring. Full cardiac monitoring may be required for other indications such as,

- infants born at <32 weeks' who required respiratory support previously and is on caffeine.
- those on respiratory support such as high flow oxygen (except low flow oxygen)
- receiving a blood transfusion
- otherwise required as per clinical decision (e.g., cardiac anomalies, arrythmias).

If an infant is on cardiac monitoring, it can be discontinued when caffeine is stopped, unless otherwise required. Oxygen saturation and heart rate monitoring can be stopped when the infant remains apnoea free two days after stopping the caffeine.

Infants who are not on caffeine treatments and do not need any respiratory support may have their cardiac monitoring stopped. If they remain asymptomatic (free of clinically significant apnoea, desaturations and bradycardia) for 2 days, oxygen saturation monitoring can be discontinued.

Apnoea monitors are no longer available in the neonatal unit and are not for use routinely. Infants who are not on continuous monitoring should have respiratory rate, heart rate, colour and temperature recorded with every feed, except for infants rooming in whereby 12 hourly is acceptable. Any concerns should prompt a full set of observations including oxygen saturations and blood pressure, and a review by the medical team. Special care rooms where an infant is not monitored MUST NOT be left unattended. A member of staff should always be present in the room.

3.4.6 Preparation and administration

Caffeine citrate 10mg/ml in 1ml ampoules – suitable for IV & oral administration

- IV infusion – may be diluted 50:50 with sodium chloride 0.9% or glucose 5%
- Loading dose: infused over 30 minutes
- Maintenance dose – give slowly over 10 min as per the BNFc but may be given faster (over 3-5 minutes) in babies who are on cardiac monitoring. Bolus administrationmay cause sudden changes in blood pressure
- Oral – use the injection orally – use filter straw

Compatibilities: The injection is compatible with sodium chloride 0.9%, glucose 5% and glucose 4% sodium chloride 0.18%.

3.5 Management of apnoea unresponsive to caffeine treatment

- Consider other causes of frequent/recurrent apnoea
- Use nasal CPAP to support breathing, may need further respiratory support i.e. mechanical ventilation

4 References (including any links to NICE Guidance etc.)

1 Schmidt B, Roberts RS, Davis P, *et al.* Caffeine therapy for apnea of prematurity. *N Engl J Med*. 2006;354:2112–21.

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4 Henderson-Smart DJ, Davis PG. Prophylactic methylxanthines for endotracheal extubation in preterm infants. *Cochrane Database Syst Rev*. Published Online First: 8 December 2010. doi: 10.1002/14651858.CD000139.pub2

5 Sand L, Szatkowski L, Kwok TC, *et al.* Observational cohort study of changing trends in non-invasive ventilation in very preterm infants and associations with clinical outcomes. *Arch Dis Child Fetal Neonatal Ed*. 2021;fetalneonatal-2021-322390.

6 Bruschettini M, Brattström P, Russo C, *et al.* Caffeine dosing regimens in preterm infants with or at risk for apnea of prematurity. *Cochrane Database Syst Rev*. 2023;2023. doi: 10.1002/14651858.CD013873.pub2

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5 Appendices

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