Management of apnoea on the neonatal unit
Full Clinical Guideline – Derby only

Reference no.: NIC RC 02/May 21/v004

1. Introduction

Apnoea is defined as cessation of breathing for more than 20 seconds. It can occur in newborn infants due to a number of conditions. 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 is presumed to be caused by the immaturity of the central respiratory control systems.

2. Aim and Purpose

- Diagnosis, investigations, and management of apnoea in newborn infants
- Use of caffeine for management of apnoea of prematurity
- Guidance for heart rate and oxygen saturation monitoring for apnoea, bradycardia, and oxygen desaturations

3. 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.

4. Main body of Guidelines

Infants who have frequent episodes of apnoea, especially when these episodes are associated with bradycardia and/or desaturations, and/or need physical stimulation or positive pressure ventilation to recover, must be clinically 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 of respiratory 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.

Treatment of apnoea of prematurity

Caffeine is the most commonly used treatment for apnoea of prematurity. It reduces the frequency 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 between the groups as 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 (3).

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.

Indication for caffeine therapy

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

Treatment regimen

Route of administration

Oral or intravenous (IV); oral route is preferred in infant is on enteral feeds

Loading dose

20 mg/kg caffeine citrate

Maintenance dose

5 mg/kg caffeine citrate once daily starting 24 hours after the loading dose. Can be increased to 10 mg/kg once daily if required.

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%

and infused over 10 minutes
- IV bolus – give slowly (over 3-5 minutes), undiluted. Bolus administration may 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%.

Monitoring caffeine levels

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 further guidance)

Stopping caffeine

Caffeine has a long half-life and can be abruptly stopped. Caffeine can be stopped in infants who are over 34 weeks corrected gestational age and are no longer having apnoea.

Heart rate and oxygen saturation monitoring

Infants having apnoea, bradycardia, or desaturations, and those of caffeine therapy should be monitored with continuous heart rate and oxygen saturation monitoring.

Cardiac monitoring can be discontinued when caffeine is stopped. Oxygen saturation monitoring can be stopped when the infants remains free of apnoeic episodes two days after stopping the caffeine treatment.

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, colour, tone, and temperature recorded with every feed (3-4 hourly). 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.

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

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

1. Schmidt B, Roberts RS, Davis P, Doyle LW, Barrington KJ, Ohlsson A, et al. Caffeine therapy for apnea of prematurity. N Engl J Med. 2006;354(20):2112-21.

2. Schmidt B, Anderson PJ, Doyle LW, Dewey D, Grunau RE, Asztalos EV, et al. Survival without disability to age 5 years after neonatal caffeine therapy for apnea of prematurity. JAMA. 2012;307(3):275-82.

3. Schmidt B, Roberts RS, Anderson PJ, Asztalos EV, Costantini L, Davis PG, et al. Academic Performance, Motor Function, and Behavior 11 Years After Neonatal Caffeine Citrate Therapy for Apnea of Prematurity: An 11-Year Follow-up of the CAP Randomized Clinical Trial. JAMA Pediatr. 2017;171(6):564-72.

4. Henderson-Smart DJ, Davis PG. Prophylactic methylxanthines for endotracheal extubation in preterm infants. Cochrane Database Syst Rev. 2010(12):CD000139.

6. Documentation Controls

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