South West Neonatal Network Guideline

Guideline for Caffeine Use in Preterm Infants

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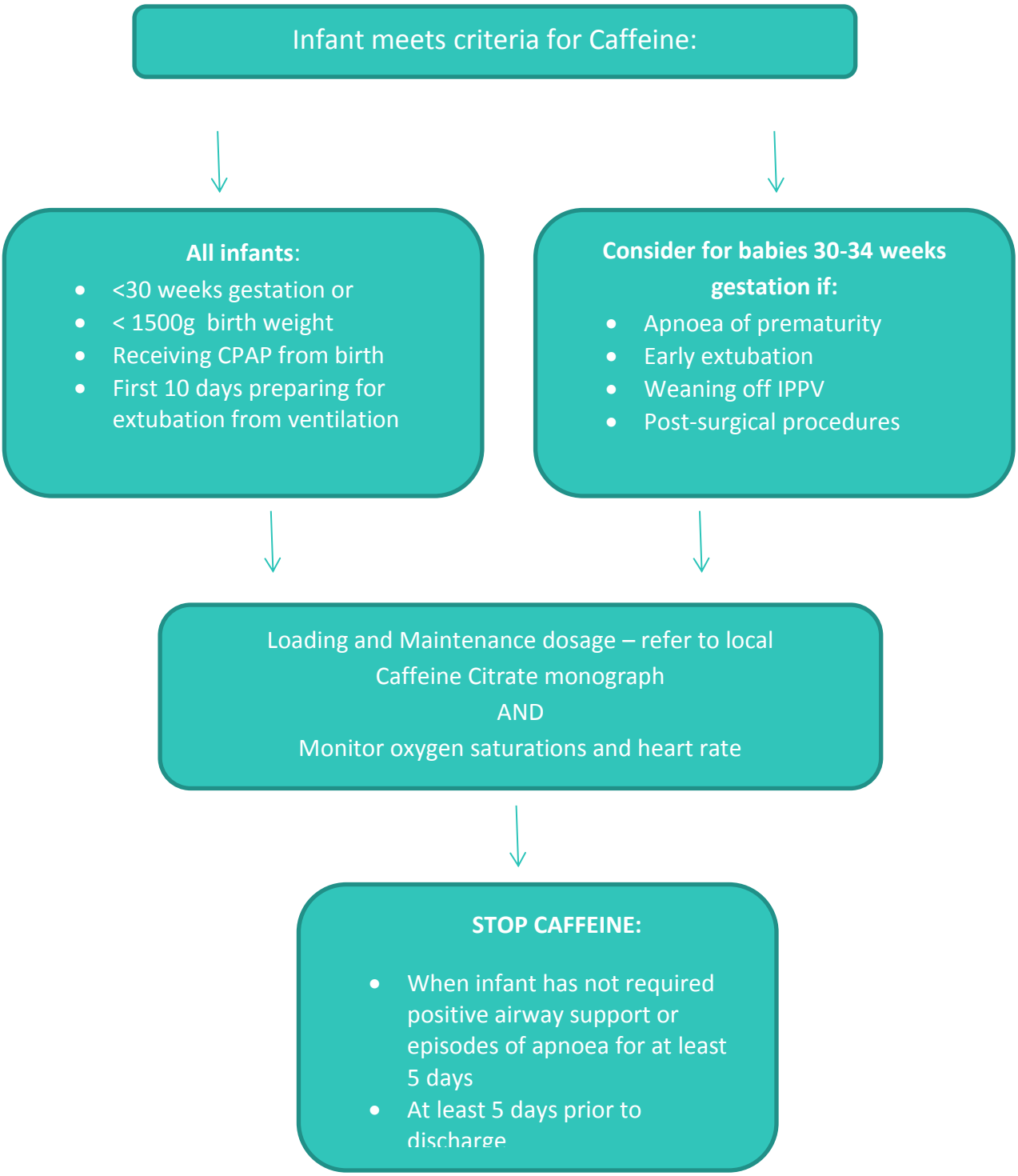
1. Overview – Guideline for Caffeine use in Preterm Infants



2. Scope

This guidelines applies to neonatal units that fall within the South West Neonatal Network

3. Definition of Terms

Prematurity	Born Before 37 Weeks' Gestation
CPAP	Continuous Positive Airway Pressure
MRI	Magnetic Resonance Imaging

4. Guideline for Caffeine Use in Preterm Infants

Introduction

- Apnoea of prematurity is defined as periods over 20 seconds of apnoea or less if associated with bradycardia and desaturation.
- Apnoea of prematurity is common but infants should be assessed to exclude other causes of apnoea such as sepsis, anaemia, NEC, encephalopathy, respiratory illness or apnoea secondary to medication.
- Methyl Xanthines (Caffeine, aminophylline and theophylline) are used as respiratory stimulants to prevent apnoea and facilitate extubation. They stimulate the respiratory centre and increase the basal metabolic rate.
- Caffeine has a long half-life of around 100 hours, thus it can be safely given once daily and has less toxicity than the other Methyl Xanthines. It has a wider therapeutic to toxic ratio and has reliable enteral absorption.

Potential Benefits:

- Reduction in apnoea[2].
- Reduction in chronic lung disease[3,4].
- Improvement in extubation failure within 7 days[5].
- Prevention of postoperative apnoea[6].
- Diuretic effect.
- Reduction, although not statistically significant, in the incidence of severe retinopathy of prematurity.
- Improved rate of survival without neuro-developmental disability at 18-21months[7] corrected. This statistically significant improvement has not been shown to persist at 5 years, although there was a continuing reduction in severity of motor impairment[8].
- Improved white matter structure on MRI[9].

Potential Risks/Disadvantages:

- Tachycardia, agitation, tachypnoea, tremors, vomiting, jitteriness and seizures (symptoms of Caffeine toxicity).
- Potential to worsen gastro-oesophageal reflux.
- Transient decreased weight gain (first 3 weeks of life).
- No significant difference in death rate, severe hearing loss[7] or necrotising enterocolitis[3] but some studies have suggested a reduction in intestinal and cerebral blood flow[10].
- Possible association with nephrocalcinosis, particularly in conjunction with diuretic therapy[11].

Treatment Criteria:

Although there is no firm evidence it is suggested that Caffeine should be commenced in all infants[12].

- Less than 30 weeks gestation, or
- Birth weight less than 1500g.

This should be started immediately in babies receiving CPAP from birth and within the first 10 days during the process of preparing for extubation in ventilated babies.

Consider starting in 30-34 week gestation infants for:

- Apnoea of prematurity.
- Facilitating early extubation – aim to start 24hrs prior to planned extubation and within 6hrs of an unplanned extubation[1].
- To wean off from positive pressure ventilation.
- Post-surgical procedures – as at increased risk of apnoeas[6].

Monitoring

- Babies receiving Caffeine should have saturation and/or ECG monitoring.
- Monitoring can be discontinued 48 hours after Caffeine is stopped if clinically appropriate.

Dosage and Regimen:

Refer to local Caffeine citrate monograph (drugs folder/intranet).

- Loading dose: 20mg/kg intravenous (or oral if tolerating more than half fluid requirement as feed).
- Maintenance dose: 5-10mg/kg intravenously or oral, once daily, 24 hours after loading dose.
- Review dose with weekly weight increase.

Routine levels are not required but consider checking if there is poor response to dosage increase or signs of possible toxicity[13].

Stop Caffeine:

- When the infant has tolerated at least 5 consecutive days without positive pressure support.
- When the infant is free of apnoea for 5 days.
- At least 5 days prior to discharge.

5. Monitoring Effectiveness

Audit Standards

- Prescribed dose of Caffeine citrate.
- Gestation when Caffeine commenced.
- Discontinuation of Caffeine when infant has not required positive airway pressure support or episodes of apnoea for at least 5 days.
- Discontinuation of Caffeine at least 5 days prior to discharge.

6. References:

[1]Steer P-A, Flenady VJ, Shearman A et al. Periextubation Caffeine in preterm neonates: A randomised dose response trial, J Paediatr. Child Health (2003) 39, 511-515.

[2]Henderson-Smart DJ, Steer P. Methylxanthine treatment for apnea in preterm infants. Cochrane database Syst Rev 2010 Issue 12 No CD000140

[3]Schmidt B, Roberts RS, Davis P et al. Caffeine therapy for Apnea of Prematurity, N Engl J Med 2006; 354:2112-21

[4]Gray PH, Flenady VJ, Charles BG, Steer PA. Caffeine citrate for very preterm infants: Effects on development, temperament and behaviour. Journal of Paediatrics and Child Health 2011; 47:167-172

[5]Henderson-Smart DJ, Davis PG. Prophylactic methylxanthines for extubation in preterm infants Cochrane database Syst Review 2010 Issue 12: No. CD00139

[6]Henderson-Smart DJ, Steer P. Postoperative Caffeine for preventing apnea in preterm infants. Cochrane Database Syst Review, 2011 CD000048

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[8] Schmidt B, Anderson PJ, Doyle LW et al. Caffeine for apnea of prematurity (CAP) trial investigators. Survival without disability to age 5 years after neonatal Caffeine therapy for apnea of prematurity. JAMA 2012 Jan 18;307(3):275-82

[9]Doyle LW, Cheong J et al. Caffeine and brain development in very preterm infants. Ann Neurol 2010;68:734-742

[10]Hoecker C. Nelle M, Poeschl J et al. Caffeine impairs cerebral and intestinal blood flow velocity in preterm infants. Pediatrics. 2002 May:109(5):784-7

[11]Zanardo V, Dani C, Trevisanuto D et al. Methylxanthines increase renal calcium excretion in preterm infants. Biol Neonate. 1995;68(3):169-74

[12] Potentially Better Practice Methylxanthines PBP#4 from NICQ 2005. TLC Exploratory Group.

[13] Leon AEC, Michienzi K et al. Serum Caffeine concentrations in preterm neonates. American Journal of Perinatology. Jan 2007, 24/1:39-47

Appendix One – Caffeine Citrate Drug Monograph

CAFFEINE CITRATE

Intravenous/oral

PRESENTATION:

Caffeine citrate 10mg/ml, 1ml ampoule.
Caffeine citrate 10mg/ml, 5ml vial for oral use.
Peyona® (caffeine citrate) 20mg/ml), 1ml ampoule.

NB Caffeine citrate 2mg = caffeine base 1mg.
NB the products are not equivalent concentrations, check carefully.

USUAL DOSAGE:

Loading dose: 20mg/kg intravenously or orally if tolerating more than half fluid requirement as feed.

Maintenance dose: 5-10mg/kg intravenously or orally once daily, 24 hours after the loading dose.

RECONSTITUTION:

Already in solution.

ADMINISTRATION:

- Loading dose should be given over 30 minutes as an intravenous infusion or orally.
- Maintenance dose should be given over 10 minutes as an intravenous dose or orally.
- For infusion it may be diluted with sodium chloride 0.9% or glucose 5%.
- Flush line with 0.5ml of sodium chloride 0.9% between each drug.

pH: 2.5 (10mg/ml) when diluted with an equal quantity of sodium chloride 0.9%.

4.4 (20mg/ml) when diluted with an equal quantity of sodium chloride 0.9%.

ADDITIONAL INFORMATION:

- It is recommended that the solution, from the ampoules, is filtered prior to use. **Once solution drawn up from ampoules it must be transferred to an oral syringe if for oral dosage.**
- The solution is acidic and should not be given intramuscularly.
- In some cases maintenance doses of higher than 10mg/kg/day (expressed as caffeine citrate) may be required to achieve maximal efficacy.
- Intravenous administration should be by slow infusion rather than bolus injection to avoid sudden changes in blood pressure.
- Routine levels are not required but consider checking if there is poor response to dosage increase or signs of toxicity. Samples do not need to be collected at any set time.

Reference sources used:

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4. *http://www.medicines.org.uk/emc/ accessed 15.03.16.*
5. *Guideline for Caffeine use in Preterm Infants Jan 2016, South West Neonatal Network.*