The Hierarchy of Evidence

The Hierarchy of evidence is based on summaries from the National Health and Medical Research Council (2009), the Oxford Centre for Evidence-based Medicine Levels of Evidence (2011) and Melynyk and Fineout-Overholt (2011).

I Evidence obtained from a systematic review of all relevant randomised control trials.

II Evidence obtained from at least one well designed randomised control trial.

III Evidence obtained from well-designed controlled trials without randomisation.

IV Evidence obtained from well designed cohort studies, case control studies, interrupted time series with a control group, historically controlled studies, interrupted time series without a control group or with case- series

V Evidence obtained from systematic reviews of descriptive and qualitative studies

VI Evidence obtained from single descriptive and qualitative studies

VII Expert opinion from clinicians, authorities and/or reports of expert committees or based on physiology

Melynyk, B. & Fineout-Overholt, E. (2011). Evidence-based practice in nursing & healthcare: A guide to best practice (2nd ed.). Philadelphia: Wolters Kluwer, Lippincott Williams & Wilkins.

National Health and Medical Research Council (2009). NHMRC levels of evidence and grades for recommendations for developers of guidelines (2009). Australian Government: NHMRC. http://www.nhmrc.gov.au/_files_nhmrc/file/guidelines/evidence_statement_form.pdf

OCEBM Levels of Evidence Working Group Oxford (2011).The Oxford 2011 Levels of Evidence. Oxford Centre for Evidence-Based Medicine. http://www.cebm.net/index.aspx?o=1025

Databases searched:	☒ CINAHL (Ebsco)	☒ Medline (Ebsco)	☒ Pubmed (NLM)	☒ Nursing (Ovid)	☒ Emcare (Ovid)
Keywords used:	Apnoea, Prematurity, Neonatal				
Search limits:	English, year 2014- Present, Peer reviewed, Full text				
Other search comments:					

2017 Nursing Clinical Effectiveness Committee
Co-Chairs: Fiona Newall & Sharon Kinney
Contact: Nursing.Research@rch.org.au

Reference (include title, author, journal title, year of publication, volume and issue, pages)	Evidence level (I-VII)	Key findings, outcomes or recommendations
Marques. K, Roehr.C.C, Brushettini. M, Davis.P, Soll.R, Methylxanthine for the Prevention and Treatment of apnea in Preterm Infants- Protocol (2021) Cochrane Database of Systematic Reviews.	I	• Apnoea often coexists with gastroesophageal reflux in preterm infants. • Episodes of apnoea can result in hypoxemia and bradycardia requiring intermittent positive pressure ventilation to support the infants's respiratory rate during periods of apnoea. • Methylxanthines are used both to treat and prevent apnoea (such as theophylline, aminophylline and caffeine)
Safer Care Victoria (2018) Apnoea https://www.safercare.vic.gov.au/clinical-guidance/neonatal/apnoea	II	• Contributing factors for apnoea: anatomical anomalies of the upper airway, sepsis, temperature disturbance, metabolic, haematological, pulmonary, CVS, CNS, prenatal and postnatal medications • Apnoea occurs in most infants <30 weeks, about 50% of infants 30-32 weeks, about 10 % of infants at 34 weeks • Management of acute apnoeic episode: Position neck in neutral position (consider prone position if full cardiorespiratory monitoring) Stimulate baby by rubbing of the soles of feet or back, aspirate airway, commence bag and mask ventilation (increase concentration of oxygen by steps of 5-10 %), use ongoing PPV if still no respiratory effort

Aggarwal, R., Singhal, A., Deorari, A., Paul, V.K. (2009). Apnoea in the newborn. *All India Institute of Medical Sciences*	VII	• Further potential causes of apnoea • Differential diagnosis • Clinical examination • Pharmacology
Atkinson, E. & Fenton, A. (2009). Management of apnoea and bradycardia in neonates. *Paediatrics and Child Health.* 19(12), 550-554	V	• Incidence of apnoea of prematurity at different gestations • Further potential causes of apnoea
Elder, D. E., Campbell, A. J. and Galletly, D. (2013), Definitions for neonatal apnoea. J Paediatr Child Health, 49: E388-E396. doi:10.1111/jpc.12247	II	• Evidence on lack of evidence based definitions of apnoea.
Gray, P.H., Flenady, V.J., Charles, B.G., Steer, P.A. (2011). Caffeine citrate for very preterm infants: effects on development, temperament and behavior. *Journal of Paediatrics and Child Health*. 47, 167-172	II	• Caffeine has similar short term effects on apnea/bradycardia as theophylline but caffeine has certain therapeutic advantages over theophylline. • Theophylline associated with higher rates of toxicity • Possibility that higher dose caffeine might be more effective in extremely preterm infants- needs further evaluation in randomized controlled trials

Henderson-Smart, D.J., Steer, P.A. (2010). Caffeine versus theophylline for apnea in preterm infants. *Chochrane Database Syst Rev*. Jan 20; (1)	I	• Caffeine has similar short term effects on apnea/bradycardia as theophylline but caffeine has certain therapeutic advantages over theophylline. • Theophylline associated with higher rates of toxicity • Possibility that higher dose caffeine might be more effective in extremely preterm infants- needs further evaluation in randomized controlled trials
Johnson, P.J. (2011). Caffeine Citrate Therapy for Apnoea of Prematurity. *Neonatal Network.* 30(6), 408-412	VII	• Review of history of methylxanthine therapy as a treatment of AOP • Examines benefits of caffeine citrate • Review of pharmacology and pharmacokinetics of caffeine • Review of current evidence-based practice for the use of caffeine citrate in treating apnoea of prematurity
Mohammed, S., Nour, I., Shabaan, A.E., |Shouman, B., Adbel-Hady, H., Nasef, N. (2015). High vs low-dose caffeine for apnea of prematurity: a randomized controlled trial. *Eur J Pediatrics*. Jul; 174(7): 949-956	II	• Shows that a higher dose of caffeine (40mg/kg load and 20mg/kg/day compared to the current standard of 20mg load and 10mg/kg/day) can decreases the chance of extubation failure and frequency of apnoeas in the preterm infant.
Powell MB, Ahlers-Schmidt CR, Engel M, Bloom BT. (2017). Clinically significant cardiopulmonary events and the effect of definition standardization on apnea of prematurity management. J Perinatol. 37:88–90. (PubMed: 27684421)	IV	• Standardizing definitions, assessments and treatment reduced the use of caffeine and home apnoea monitors upon NICU discharge

Salatin. J-P, de Queiroz. M, Orliaguet. G. (2020) Development: Epidemiology and management of postoperative apnoea in premature and term newborns. SFAR.	VII	• Postoperative monitoring for apnoea • Recommendations of postoperative monitoring of infants at risk of apnoea • Suggestion for protocol changes for monitoring infants at risk of apnoea postoperatively
Schmidt B, Roberts RS, Anderson PJ, et al. (2017). Academic Performance, Motor Function, and Behavior 11 Years After Neonatal Caffeine Citrate Therapy for Apnea of PrematurityAn 11-Year Follow-up of the CAP Randomized Clinical Trial. JAMA Pediatr. 171(6):564–572. doi:10.1001/jamapediatrics.2017.0238	II	• Caffeine reduced risk of motor impairment in 11-year-old children with very low birth weight. • Neonatal caffeine therapy is effective and safe into middle school age.
Sreenan, C., Lemke, R.P., Hudson-Mason, A., Osiovich, H. (2001). High-flow nasal cannulae in the management of apnoea of prematurity: A comparison with conventional nasal continuous positive airway pressure. *Pediatrics* 107, 1081-1083	IV	• Comparison of CPAP and high-flow nasal cannula (HFNC) oxygen in the management of AOP • At flows of 2.5L/min in infants <2kg, HFNC can generate positive distending pressure which is as effective as NCPAP in the management of AOP
Zhao, J., Gonzalez, F. & Mu, D. Eur J Pediatr (2011) 170: 1097. https://doi.org/10.1007/s00431-011-1409-6	VII	• Discussion of Neonatal apnoea, investigations, treatment and management