VENTILATION: CONTINUOUS POSITIVE AIRWAY PRESSURE (CPAP)
Supporting information

This guideline has been prepared with reference to the following:

NICE. Specialist neonatal respiratory care for babies born preterm - quality standard. 2020. London. NICE

https://www.nice.org.uk/guidance/qs193

NICE. Specialist neonatal respiratory care for babies born preterm – clinical guideline. 2019. London. NICE

https://www.nice.org.uk/guidance/ng124

What are the indications for CPAP?

Recurrent spells of apnoea (pause in breathing > 20 seconds) are "almost universal" in infants < 34 weeks' gestation (Lemyre, 2002). CPAP is used to support these infants, along with those recently extubated or with respiratory distress soon after birth (De Paoli, 2007). Pao_2 < 50-60 mm Hg whilst breathing > 40%-70% oxygen is regarded as a positive indication for CPAP in most units (Carlo, 2001).

A small retrospective randomised study (Dani, 2004) compared nasal CPAP with mechanical ventilation (MV) following surfactant therapy and extubation in preterm infants with respiratory distress syndrome. In the MV group, 6 patients (43%) were still dependent on MV at 7 days of life, vs no patients in the CPAP group.

Nasal CPAP reduces the incidence of adverse effects after extubation including failure (NNT 6; 95% CI 4-15) and chronic lung disease at 28 days (NNT 6; 95% CI 3-22) (Halliday, 2004).

Data from a comparison of treatment of premature infants at the University of Vienna tertiary centre and the Vermont Oxford Neonatal Network as a whole (Kirchner, 2005) is also suggestive of an improved rate of retinopathy of prematurity (1-10% vs 8-12%) as well as chronic lung disease (14-32% vs 27-39%), when CPAP is used more often (45-86% vs 37-63%).

A randomised, multicentre trial in 1316 infants (Finer, 2010) assigned babies to intubation and surfactant treatment (within 1 hour after birth) or to CPAP treatment initiated in the delivery room, with subsequent use of a protocol-driven limited ventilation strategy. Infants were also randomly assigned to one of two target ranges of oxygen saturation. The primary outcome was death or bronchopulmonary dysplasia as defined by the requirement for supplemental oxygen at 36 weeks (with an attempt at withdrawal of supplemental oxygen in neonates who were receiving less than 30% oxygen). The rates of the primary outcome did not differ significantly between the CPAP group and the surfactant group (47.8% and 51.0%, respectively; relative risk with CPAP, 0.95; 95% CI, 0.85 to 1.05) after adjustment for gestational age, centre, and familial clustering. The results were similar when bronchopulmonary dysplasia was defined according to the need for any supplemental oxygen at 36 weeks (rates of primary outcome, 48.7% and 54.1%, respectively; relative risk with CPAP, 0.91; 95% CI, 0.83 to 1.01). Infants who received CPAP treatment, as compared with infants who received surfactant treatment, less frequently required intubation or postnatal corticosteroids for bronchopulmonary dysplasia (P<0.001), required fewer days of mechanical ventilation (P=0.03), and were more likely to be alive and free from the need for mechanical ventilation by day 7 (P=0.01). The rates of other adverse neonatal outcomes did not differ significantly between the two groups. The authors concluded that CPAP was a viable alternative to intubation and surfactant in preterm infants.

Carlo WA. Assisted ventilation. In: Klaus MH, Fanaroff AA (eds). Care of the high-risk neonate, 5th ed. Philadelphia, W.B. Saunders, 2001. p.282

Dani C, Bertini G, Pezzati M, et al. Early extubation and nasal continuous positive airway pressure after surfactant treatment for respiratory distress syndrome among preterm infants <30 weeks' gestation. Pediatrics 2004;113:e560-3
http://pediatrics.aappublications.org/content/113/6/e560.long

De Paoli AG, Davis PG, Faber B, et al. Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates. The Cochrane Database of Systematic Reviews 2007, Issue 3. Art. No.: CD002977
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002977.pub2/full

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Finer NN, Carlo WA, Walsh MC, et al. Early CPAP versus surfactant in extremely preterm infants. New Engl J Med 2010;362:1970-9
http://www.nejm.org/doi/full/10.1056/NEJMoa0911783#t=articleTop

Halliday HL. What interventions facilitate weaning from the ventilator? A review of the evidence from systematic reviews. Paediatr Respir Rev 2004;5(Suppl A):S347-52

Kirchner L, Weninger M, Unterasinger L, et al. Is the use of early nasal CPAP associated with lower rates of chronic lung disease and retinopathy of prematurity? Nine years of experience with the Vermont Oxford Neonatal Network. J Perinat Med 2005;33:60-6

Lemyre B, Davis PG, De Paoli AG. Nasal intermittent positive pressure ventilation (NIPPV) versus nasal continuous positive airway pressure (NCPAP) for apnea of prematurity. The Cochrane Database of Systematic Reviews 2002, Issue 1. Art. No.: CD002272
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002272/full

Evidence Level: I

What pressure range should be used?

A 2021 systematic review of RCTs was unable to determine the optimal pressure level of nasal CPAP in preterm infants to prevent morbidity of mortality (Bamat, 2021). This review compared 'low' (≤ 5 cm H2O) versus 'moderate-high' (> 5 cm H2O) nasal CPAP pressure levels. Results showed statistically insignificant results for death or bronchopulmonary dysplasia (BPD) at 36 weeks' postmenstrual age (PMA) (risk ratio (RR) 1.02, 95% confidence interval (CI) 0.56 to 1.85; 1 trial, 271 participants); mortality by hospital discharge (RR 1.04, 95% CI 0.51 to 2.12; 1 trial, 271 participants); BPD at 28 days of age (RR 1.10, 95% CI 0.56 to 2.17; 1 trial, 271 participants); BPD at 36 weeks' PMA (RR 0.80, 95% CI 0.25 to 2.57; 1 trial, 271 participants), and treatment failure or need for mechanical ventilation (RR 1.00, 95% CI 0.63 to 1.57; 1 trial, 271 participants), need for mechanical ventilation (RR 1.52, 95% CI 0.92 to 2.50; 2 trials, 117 participants).

Conventionally, a nasal CPAP of 5 cm H_2O is used, rising in 1 cm increments to 10 cm. if there is no improvement. Higher levels may over-distend the lungs, leading to hypercapnia (De Paoli, 2007; Carlo, 2001).

Bamat N, Fierro J, Mukerji A et al. Nasal continuous positive airway pressure levels for the prevention of morbidity and mortality in preterm infants. Cochrane Database Syst Rev. 2021;11:CD012778
https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD012778.pub2/full

Carlo WA. Assisted ventilation. In: Klaus MH, Fanaroff AA (eds). Care of the high-risk neonate, 5th ed. Philadelphia, W.B. Saunders, 2001. p.283

De Paoli AG, Davis PG, Faber B, et al. Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates. The Cochrane Database of Systematic Reviews 2007, Issue 3. Art. No.: CD002977
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002977.pub2/full

Evidence Level: I

How should infants be weaned from CPAP?

A 2020 systematic review concluded that a strategy of gradual weaning of airway pressure might increase the chances of successful weaning (van Delft, 2020). Stepdown strategy from CPAP to nasal cannula is a useful alternative resulting in an earlier weaning, but the focus should remain on continued weaning in order to avoid prolonged oxygen supplementation. Interval training should probably not be used. The meta analysis showed that with gradual pressure wean, the relative risk of successful weaning at the first attempt was 1.30 (95% CI 0.93 to 1.83), as compared with sudden discontinuation. Infants were weaned at a later postmenstrual age (PMA) (median difference (MD) 0.93 weeks (95% CI 0.19 to 1.67)). A stepdown strategy to nasal cannula resulted in an almost 3-week reduction in the PMA at successful weaning (MD −2.70 (95% CI −3.87 to −1.52)) but was associated with a significantly longer duration of oxygen supplementation (MD 7.80 days (95% CI 5.31 to 10.28)). A strategy using interval training had no clinical benefits. None of the strategies had any effect on the risk of chronic lung disease or the duration of hospital stay.

A Cochrane systematic review of 3 trials (Jardine 2011) concluded that: “Infants who have their NCPAP pressure weaned to a predefined level and then stop NCPAP completely have less total time

on NCPAP and shorter durations of oxygen therapy and hospital stay compared with those that have NCPAP removed for a predetermined number of hours each day. Future trials of withdrawing NCPAP should compare proposed strategies with weaning NCPAP pressure to a predefined level and then stopping NCPAP completely. Clear criteria need to be established for the definition of stability prior to attempting to withdraw NCPAP."

Jardine LA, Inglis GD, Davies MW. Strategies for the withdrawal of nasal continuous positive airway pressure (NCPAP) in preterm infants. Cochrane Database of Systematic Reviews 2011, Issue 2. Art. No.: CD006979
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD006979.pub2/full

van Delft B, van Ginderdeuren F, Lefevere J et al. Weaning strategies for the withdrawal of non-invasive respiratory support applying continuous positive airway pressure in preterm infants: a systematic review and meta-analysis. BMJ Paediatr Open. 2020;4:e000858
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7678397/

Evidence Level: I

What types of CPAP are available?

The two most widely-used systems are conventional nasal CPAP and the Infant Flow Driver system. Conventional CPAP delivered with a conventional ventilator and nasal prongs was compared to the Infant Flow CPAP (IF CPAP) system in a prospective, randomised study of 162 intubated extremely low birth weight infants (Stefanescu, 2003). Individual extubation success rates were identical at 61.9% (52 of 84) in the CPAP group vs 61.5% (48 of 78) in the IF CPAP group. The IF CPAP group did, however, experience fewer days on supplemental oxygen and shorter hospital stays.
Short binasal prongs (as in the Infant Flow system) produce more stable pressures (De Paoli, 2007) and are more effective than single prongs in reducing the rate of re-intubation (De Paoli, 2008). New generation facemasks that are more effective than those used originally, and that cause minimal nasal trauma, have recently been developed. No clinical comparisons with nasal prongs have yet been completed (De Paoli, 2003).
A small study in 13 premature infants (Boumecid, 2007) suggests that variable-flow NCPAP increases tidal volume and improves thoraco-abdominal synchrony to a greater extent than is the case with constant-flow NCPAP and nasal prongs.

Boumecid H, Rakza T, Abazine A, et al. Influence of three nasal continuous positive airway pressure devices on breathing pattern in preterm infants. Arch Dis Child Fetal Neonatal Ed 2007;92:F298-300
http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2675435/

De Paoli AG, Morley C, Davis PG. Nasal CPAP for neonates: what do we know in 2003? Arch Dis Child Fetal Neonatal Ed 2003;88:F168-72
http://fn.bmj.com/content/88/3/F168.long

De Paoli AG, Davis PG, Faber B, et al. Devices and pressure sources for administration of nasal continuous positive airway pressure (NCPAP) in preterm neonates. The Cochrane Database of Systematic Reviews 2007, Issue 3. Art. No.: CD002977
http://onlinelibrary.wiley.com/doi/10.1002/14651858.CD002977.pub2/full

Stefanescu BM, Murphy WP, Hansell BJ, et al. A randomized, controlled trial comparing two different continuous positive airway pressure systems for the successful extubation of extremely low birth weight infants. Pediatrics 2003;112:1031-8
http://pediatrics.aappublications.org/content/112/5/1031.long

Evidence Level: II

Is bubble CPAP superior to conventional CPAP?

A 2016 RCT compared CPAP failure rates between Bubble CPAP (BCPAP) and conventional ventilator derived CPAP (VCPAP) among 68 very low birthweight babies (VLBW), with moderate respiratory distress (Agarwal, 2016). The failure rates were found to be similar whether BCPAP or ventilator VCCPAP was used (14.7% vs 32.4% p=0.08). There was no difference in complication rates of intraventricular haemorrhage (24% vs 9% p=0.10) or mortality (6% vs 9% p=0.642) with either method of CPAP.
A few earlier randomised studies have compared these two approaches (Colaizy, 2004; McEvoy, 2004; Lee, 1998) and have recorded reductions of up to 50% in the need for mechanical ventilation in favour of bubble CPAP. Another advantage is low cost: bubble CPAP equipment costs are 15% of

those for mechanical ventilation, and the technique can be administered by nursing staff (Koyamaibole, 2006).

Agarwal S, Maria A, Roy MK et al. A Randomized Trial Comparing Efficacy of Bubble and Ventilator Derived Nasal CPAP in Very Low Birth Weight Neonates with Respiratory Distress. J Clin Diagn Res. 2016;10:SC09-SC12
https://www.ncbi.nlm.nih.gov/pmc/articles/PMC5072040/

Colaizy TT, McEvoy C, Crichton C, et al. Bubble vs. conventional CPAP: a prospective, randomized, pilot study. Pediatr Res 2004;55:80

Koyamaibole L, Kado J, Qovu JD, et al. An evaluation of bubble-CPAP in a neonatal unit in a developing country: effective respiratory support that can be applied by nurses. J Trop Pediatr 2006;52:249-53

Lee KS, Dunn MS, Fenwick M, et al. A comparison of underwater bubble continuous positive airway pressure with ventilator-derived continuous positive airway pressure in premature neonates ready for extubation. Biol Neonate 1998;73:69-75

McEvoy CT, Colaizy T, Crichton C, et al. Randomized trial of early bubble continuous positive airway pressure (BCPAP) versus conventional CPAP (CCPAP): effect on pulmonary function in preterm infants. Pediatr Res 2004;55:169

Evidence Level: II

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