B.3 CONTINUOUS POSITIVE AIRWAY PRESSURE SOURCE

Recommendation and remarks

RECOMMENDATION B.3 (NEW)

For preterm infants who need continuous positive airway pressure (CPAP) therapy, bubble CPAP may be considered rather than other pressure sources (e.g. ventilator CPAP). *(Conditional recommendation, low-certainty evidence)*

Remarks

- The recommendation is conditional on shared decision-making with parents; this includes informing parents about the benefits and risks and the need for further research.
- Evidence was derived from trials that compared underwater (water-seal) "bubble" CPAP with mechanical ventilator CPAP or Infant Flow Driver (IFD) CPAP. All trials used commercially available devices and all used humidified blended oxygen–air.
- The GDG noted that the evidence on harms (increased nasal injury) was of uncertain clinical significance and the certainty of the body of evidence was low due to bias and imprecision.
- The GDG suggested that the nasal interfaces (i.e. prongs and cannulas) used with bubble CPAP machines should be carefully selected and that skilled nursing care is needed for the prongs and cannulas.
- The GDG also considered that careful selection, maintenance and monitoring of bubble CPAP devices is needed. Only commercially available bubble CPAP devices should be used; locally-manufactured or locally-adapted bubble CPAP devices should not be used.

Background and definitions

There are many different types of CPAP machines and pressure generation for ventilatory support of preterm infants. There is also considerable variation in practice and differing reports of benefits and harms *(150,160,161)*. The older-style CPAP pressure sources were mechanical ventilators; newer types include Infant Flow Driver (IFD) and bubble CPAP. Bubble CPAP uses an underwater water-seal method and is commonly used for providing CPAP to babies in LMICs *(150,160,161)*.

Summary of the evidence

OVERVIEW	B.3 Continuous positive airway pressure source
PICO	**Population** – Preterm infants with respiratory distress syndrome or post-extubation **Intervention** – Bubble CPAP pressure source **Comparator** – Other CPAP pressure sources (ventilator CPAP or Infant Flow Driver CPAP) **Outcomes** – All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up
Timing, setting, subgroups	**Timing of the intervention** – Immediately after birth **Setting** – Health-care facility or home in any country or setting **Subgroups** • Gestational age at birth (< 32 weeks, ≥ 32 weeks) • Birth weight (< 1.5 kg, ≥ 1.5 kg)

Effectiveness: Comparison – Bubble CPAP versus other CPAP pressure sources

Sources and characteristics of the evidence

The effectiveness evidence was derived from a systematic review of 15 RCTs including a total of 1437 preterm infants *(162)*. Most trials were small (median number of participants 88 [IQR 39–140]). They were conducted over the past 25 years in neonatal centres in seven countries (Albania, Armenia, Brazil, India, the Islamic Republic of Iran, Italy and the United Kingdom). The inclusion criteria were infants who required primary treatment for RDS after birth or following a period of mechanical ventilation (post-extubation). Most infants were born before 32 weeks' gestation (very preterm). Thirteen trials included both RDS and post-extubation infants, two trials included infants with RDS only and no trials included post-extubation infants only. All trials compared bubble CPAP with ventilator or IFD CPAP devices. The devices were all commercially manufactured; no locally manufactured or locally adapted devices were used. The interfaces in all trials were short nasal prongs. All infants received standard supportive care (i.e. supplemental oxygen).

Critical outcomes

For bubble CPAP compared with ventilator or IFD nasal CPAP, 10 trials reported all-cause mortality, 14 reported morbidity (13 reported "treatment failure", 14 pneumothorax, 7 bronchopulmonary dysplasia and 8 nasal injury). No trials reported growth or neurodevelopment. (Full details are provided in GRADE Table B.3, in the Web Supplement.)

- **Mortality:** Low-certainty evidence from 10 trials totalling 1189 participants suggests little or no effect on all-cause mortality by hospital discharge (RR 0.93, 95% CI 0.64 to 1.36).
- **Morbidity/adverse events:** Low-certainty evidence from 13 trials totalling 1230 participants suggests a decrease in "treatment failure" (defined as recurrent apnoea, hypoxia, hypercarbia, increasing oxygen requirement, or the receipt of mechanical ventilation within 72 hours after initiation of nasal CPAP) by hospital discharge (RR 0.76, 95% CI 0.60 to 0.95). Low-certainty evidence from 14 trials totalling 1340 participants suggests a decrease in pneumothorax (RR 0.73, 95% CI 0.40 to 1.34). Low-certainty evidence from seven trials totalling 603 participants suggests a decrease in bronchopulmonary dysplasia (oxygen dependency at 28 days) (RR 0.76, 95% CI 0.53 to 1.10). Low-certainty evidence from eight trials of 753 participants suggests an increase in nasal injury (defined as ulceration, bleeding, septal injury and scarring but excluding hyperaemia and erythema) by hospital discharge (RR 2.29, 95% CI 1.37 to 3.82).

Other outcomes

There was a decrease in length of hospital stay (in days) (MD -3.27, 95% CI -4.99 to -1.56 days; 5 trials, 591 participants).

Subgroup analyses

The effect of gestational age and birth weight could not be assessed as there were insufficient trials for any critical outcome.

Values and acceptability

The systematic review about what matters to families about the care of the preterm or LBW infant (Table 1.1) reported that carers want assistance in interacting with their babies, especially when they are undergoing therapies that make it difficult to have physical contact *(14)*. They want to learn about the health-care setting where they need to stay and care for their baby. They want to understand what medical equipment is being used and why. Studies report that families can find mechanical ventilation and CPAP intimidating and frightening and that these therapies can accentuate their feelings of inadequacy and lack of control over their baby's health care *(147,159)*. Families also worry about the pain and discomfort their baby is experiencing in NICUs *(14)*. Studies from LMICs indicate that bubble CPAP is both valued and acceptable to families and health workers *(163,164)*. No other specific evidence was located about whether families value bubble CPAP rather than other types of CPAP for their preterm or LBW baby or whether they find bubble CPAP more or less acceptable.

Resources required and implementation considerations

Please refer to the information on this topic in section B.1.

Feasibility and equity

Studies from LMICs *(165-168)* report the low cost and feasibility of establishing bubble CPAP services. There was no other specific evidence on the feasibility and equity of providing CPAP for preterm or LBW infants.

Summary of judgements

Comparison: Bubble CPAP vs other CPAP pressure sources (B.3)	
Justification	• Evidence of small-to-moderate benefits: decreased pneumothorax, decreased bronchopulmonary dysplasia and decreased failed treatment (defined as recurrent apnoea, hypoxia, hypercarbia, increasing oxygen requirement or the need for mechanical ventilation) *(low-certainty evidence)* • Evidence of small harms: increased nasal injury (defined as ulceration, bleeding, septal injury and/or scarring but excluding hyperaemia and erythema) *(low-certainty evidence)* • Evidence of little or no effect on mortality *(low-certainty evidence)* • No evidence on other critical outcomes

Evidence-to-Decision summary	
Benefits	Small to moderate
Harms	Small
Certainty	Low
Balance	Probably favours bubble CPAP
Values	Uncertainty or variability about outcomes
Acceptability	Varies
Resources	Moderate
Feasibility	Varies
Equity	Varies