B.2 CONTINUOUS POSITIVE AIRWAY PRESSURE IMMEDIATELY AFTER BIRTH

Recommendation and remarks

RECOMMENDATION B.2 (NEW)

Continuous positive airway pressure (CPAP) therapy may be considered immediately after birth for very preterm infants (< 32 weeks' gestation), with or without respiratory distress. *(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.
- The GDG noted that duration of CPAP (i.e. when to stop CPAP) should be based on clinical judgement.
- The GDG also noted that skilled staff and quality equipment (including humidified blended oxygen–air) are needed for the administration of CPAP to preterm and LBW infants.

Background and definitions

The benefits of CPAP for RDS in preterm infants are well established *(151,155)*. However, it can be difficult to ascertain respiratory status in preterm babies soon after birth and to accurately predict the prognosis. Preterm babies with respiratory failure may not show signs of respiratory distress in the first hours after birth and babies with early respiratory distress may improve *(147)*. Thus, health workers in NICUs sometimes administer CPAP immediately after birth to all babies at risk, regardless of respiratory status (sometimes called immediate CPAP), rather than assessing for RDS. Benefits and harms of this practice have been unclear *(147,148,150)*. However, recent trials have assessed the effectiveness of immediate CPAP compared with both supplemental oxygen and mechanical ventilation.

Summary of the evidence

OVERVIEW	B.2a Immediate CPAP vs supplemental oxygen	B.2b Immediate CPAP vs mechanical ventilation
PICO	**Population** – Preterm infants immediately after birth **Intervention 1** – CPAP commencing immediately after birth **Comparator 1** – Supplemental oxygen by head box, face mask or nasal cannula **Outcomes** – All-cause mortality, morbidity, growth, neurodevelopment at latest follow-up	**Population** – Preterm infants immediately after birth **Intervention 2** – CPAP commencing immediately after birth **Comparator 2** – Mechanical ventilation **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) • and birth weight (< 1.5 kg, ≥ 1.5 kg)	

Effectiveness: Comparison 1 – Immediate CPAP versus supplemental oxygen

Sources and characteristics of the evidence

For this comparison, the effectiveness evidence was derived from a Cochrane systematic review of four trials enrolling a total of 765 infants under 32 weeks' gestation at birth from seven countries (Argentina, Brazil, Canada, Italy, Paraguay, Peru and Uruguay) *(158)*. An updated search conducted on 1 October 2021 located no new trials. The review found two types of trial: (i) trials that provided CPAP within 15 minutes of birth regardless of respiratory status, and (ii) trials that provided CPAP between 15 and 60 minutes after birth prior to the onset of RDS.

Critical outcomes

For comparison 1, four trials reported all-cause mortality, four reported morbidity (4 reported "failed treatment", 4 bronchopulmonary dysplasia, 1 a composite outcome of death or bronchopulmonary dysplasia, 3 pneumothorax, 2 intraventricular haemorrhage). No trials reported growth or neurodevelopment. (Full details are provided in GRADE Table B.2a, in the Web Supplement.)

- **Mortality:** Moderate-certainty evidence from four trials totalling 765 participants suggests little or no effect on all-cause mortality by hospital discharge (RR 1.09, 95% CI 0.60 to 1.96).
- **Morbidity:** Very-low-certainty evidence from four trials totalling 765 participants suggests a decreased risk of "failed treatment" (defined as recurrent apnoea, hypoxia, hypercarbia, increasing oxygen requirement, or the need for mechanical ventilation) by hospital discharge (RR 0.60, 95% CI 0.49 to 0.74). Moderate-certainty evidence from three trials totalling 683 participants suggests decreased bronchopulmonary dysplasia by 36 weeks PMA (RR 0.76, 95% CI 0.51 to 1.14). Low-certainty evidence from one trial with 256 participants suggests decreased death or bronchopulmonary dysplasia by 36 weeks PMA (RR 0.69, 95% CI 0.40 to 1.19). Low-certainty evidence from three trials totalling 568 participants suggests decreased pneumothorax by hospital discharge (RR 0.75, 95% CI 0.35 to 1.61). Low-certainty evidence from two trials totalling 486 participants suggests little or no effect on intraventricular haemorrhage grade 3 or 4 by hospital discharge (RR 0.96, 95% CI 0.39 to 2.37).

Other outcomes

Three trials reported a decrease in surfactant use by hospital discharge (RR 0.75, 95% CI 0.58 to 0.96; 3 trials, 683 participants).

Subgroup analyses

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

Effectiveness: Comparison 2 – Immediate CPAP versus mechanical ventilation

Sources and characteristics of the evidence

For this comparison, the effectiveness evidence was derived from the same Cochrane systematic review *(158)*. Three trials were included, which enrolled a total of 2364 very preterm infants (< 32 weeks' gestation) from 17 countries (Argentina, Australia, Belgium, Brazil, Canada, Chile, France, Germany, Greece, Italy, the Islamic Republic of Iran, New Zealand, Norway, Paraguay, Peru, Uruguay and the USA). An updated search conducted on 1 October 2021 located no new trials. The review included the same two types of trials as described above.

Critical outcomes

For comparison 2, four trials reported all-cause mortality, four trials reported morbidity (4 reported "failed treatment", 3 bronchopulmonary dysplasia, 1 a composite outcome of death or bronchopulmonary dysplasia, 3 pneumothorax, 2 intraventricular haemorrhage) and one trial reported on neurodevelopment (neurodevelopmental impairment). No trials reported growth. (Full details are provided in GRADE Table B.2b, in the Web Supplement.)

- **Mortality:** Moderate-certainty evidence from three trials totalling 2358 participants suggests little or no effect on all-cause mortality by hospital discharge (RR 0.82, 95% CI 0.66 to 1.03).
- **Morbidity:** Moderate-certainty evidence from two trials totalling 1042 participants suggests a decrease in risk of "failed treatment" (defined as recurrent apnoea, hypoxia, hypercarbia, increasing oxygen requirement, or the need for mechanical ventilation) by hospital discharge (RR 0.49, 95% CI 0.45 to 0.54). Moderate-certainty evidence from three trials totalling 2150 participants suggests a decrease in bronchopulmonary dysplasia at 36 weeks PMA (RR 0.89, 95% CI 0.80 to 0.99). Moderate-certainty evidence from three trials totalling 2358 participants suggests a decrease in the combined outcome of all-cause mortality and bronchopulmonary dysplasia at 36 weeks PMA (RR 0.89, 95% CI 0.81 to 0.97). Low-certainty evidence from three trials totalling 2357 participants suggests little or no effect on pneumothorax by hospital discharge (RR 1.24, 95% CI 0.91 to 1.69). Moderate-certainty evidence from three trials totalling 2301 participants suggests little or no effect on intraventricular haemorrhage grade 3 or 4 by hospital discharge (RR 1.09, 95% CI 0.86 to 1.39).
- **Neurodevelopment:** Moderate-certainty evidence from one trial with 976 participants suggests little or no effect on neurodevelopmental impairment (defined as cerebral palsy, developmental delay, intellectual impairment, blindness or sensorineural deafness) by 18–22 months of age (RR 0.91, 95% CI 0.62 to 1.32).

Other outcomes

There was decrease in surfactant use (RR 0.60, 95% CI 0.57 to 0.63; 3 trials, 2354 infants).

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 (see 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)*. No other specific evidence was located about whether families value immediate CPAP for their preterm or LBW baby or whether they find it more or less acceptable than supplemental oxygen.

Resources required and implementation considerations

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

Feasibility and equity

As described in section B.1, there was no specific evidence on the feasibility and equity of providing CPAP for preterm or LBW infants.

Summary of judgements

	Comparison 1. CPAP immediately after birth for very preterm infants vs supplemental oxygen (B2.a)	**Comparison 2. CPAP immediately after birth for very preterm infants vs mechanical ventilation (B2.a)**
Justification	In trials where most participants are very preterm (< 32 weeks' gestation): • Evidence of small benefits: decreased "failed treatment" (defined as recurrent apnoea, hypoxia, hypercarbia, increasing oxygen requirement or the need for mechanical ventilation), decreased bronchopulmonary dysplasia *(moderate-certainty evidence)* and decreased pneumothorax *(low-certainty evidence)* • No evidence of harms • Evidence of little or no effect on mortality and intraventricular haemorrhage *(moderate-certainty evidence)* • No evidence on other critical outcomes	In trials where most participants are very preterm (< 32 weeks' gestation): • Evidence of moderate benefits: decreased "failed treatment" (defined as recurrent apnoea, hypoxia, hypercarbia, increasing oxygen requirement or the need for mechanical ventilation), decreased bronchopulmonary dysplasia *(moderate-certainty evidence)* • No evidence of harms • Evidence of little or no effect on mortality *(moderate-certainty evidence)* pneumothorax *(low-certainty evidence)*, intraventricular haemorrhage *(moderate-certainty evidence)* and neurodevelopment *(moderate-certainty evidence)* • No evidence on other critical outcomes
Evidence-to-Decision summary		
Benefits	Small	Moderate
Harms	Trivial or none	Trivial or none
Certainty	Low	Moderate
Balance	Probably favours CPAP immediately after birth for very preterm infants (< 32 weeks' gestation)	Probably favours CPAP immediately after birth for very preterm infants (< 32 weeks' gestation)
Values	No uncertainty or variability about outcomes	Probable uncertainty or variability about outcomes
Acceptability	Varies	Varies
Resources	Vary	Vary
Feasibility	Varies	Varies
Equity	Varies	Varies