Nasal intermittent positive pressure ventilation (NIPPV) versus nasal continuous positive airway pressure (NCPAP) for preterm neonates after extubation (Review)

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[Intervention Review]

Nasal intermittent positive pressure ventilation (NIPPV) versus nasal continuous positive airway pressure (NCPAP) for preterm neonates after extubation

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ABSTRACT

Background

Previous randomised trials and meta-analyses have shown nasal continuous positive airway pressure (NCPAP) to be a useful method of respiratory support after extubation. However, infants managed in this way sometimes "fail" and require endotracheal reintubation with its attendant risks and expense. Nasal intermittent positive pressure ventilation (NIPPV) is a method of augmenting NCPAP by delivering ventilator breaths via nasal prongs. Older children and adults with chronic respiratory failure have been shown to benefit from NIPPV and the technique has been applied to neonates. However, serious side effects including gastric perforation have been reported and clinicians remain uncertain about the role of NIPPV in the management of neonates. It has recently become possible to synchronise delivery of NIPPV with the infant's own breathing efforts, which may make this modality more useful in this patient group.

Objectives

To determine whether the use of NIPPV when compared to NCPAP decreases the rate of extubation failure without adverse effects in the preterm infant extubated following a period of intermittent positive pressure ventilation.

Search strategy

MEDLINE was searched using the MeSH terms: Infant, Newborn (exp) and Positive-pressure respiration (exp) up to December 18, 2007. Other sources included the Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library, Issue 4, 2007), CINAHL using search terms: Infant, newborn and intermittent positive pressure ventilation, expert informants, previous reviews including cross-references and conference and symposia proceedings were used.

Selection criteria

Randomised trials comparing the use of NIPPV with NCPAP in preterm infants being extubated were selected for this review.

Data collection and analysis

Data regarding clinical outcomes including extubation failure, endotracheal reintubation, rates of apnea, gastrointestinal perforation, feeding intolerance, chronic lung disease and duration of hospital stay were extracted independently by the three review authors. The trials were analysed using relative risk (RR), risk difference (RD) and number needed to treat (NNT) for dichotomous outcomes and weighted mean difference (WMD) for continuous outcomes.

Main results

Three trials comparing extubation of infants to NIPPV or to NCPAP were identified. All trials used the synchronised form of NIPPV. Each showed a statistically significant benefit for infants extubated to NIPPV in terms of prevention of extubation failure criteria. The meta-analysis demonstrates a statistically and clinically significant reduction in the risk of meeting extubation failure criteria [typical RR 0.21 (95% CI 0.10, 0.45), typical RD -0.32 (95% CI -0.45, -0.20), NNT 3 (95% CI 2, 5)]. There were no reports of gastrointestinal perforation in any of the trials. Differences in rates of chronic lung disease approached but did not achieve statistical significance favouring NIPPV [typical RR 0.73 (95% CI 0.49, 1.07), typical RD -0.15 (95% CI -0.33, 0.03)].

Authors' conclusions

Implications for practice: NIPPV is a useful method of augmenting the beneficial effects of NCPAP in preterm infants. Its use reduces the incidence of symptoms of extubation failure more effectively than NCPAP. Within the limits of the small numbers of infants randomised to NIPPV there is a reassuring absence of the gastrointestinal side effects that were reported in previous case series.

Implications for research: Future trials should enroll a sufficient number of infants to detect differences in important outcomes such as chronic lung disease and gastrointestinal perforation. The impact of synchronisation of NIPPV on the technique's safety and efficacy should be established in future trials.

PLAIN LANGUAGE SUMMARY

Nasal intermittent positive pressure ventilation (NIPPV) versus nasal continuous positive airway pressure (NCPAP) for preterm neonates after extubation

There is some evidence that nasal intermittent positive pressure ventilation (NIPPV) increases the effectiveness of nasal continuous positive airway pressure (NCPAP) in preterm babies who no longer need an endotracheal tube (tube in the wind pipe). Preterm babies with breathing problems often require help from a machine (ventilator) that provides regular breaths through a tube in the windpipe. The process of extubation or removal of this tube does not always go smoothly and the tube may need to go back if the baby cannot manage by him/herself. NCPAP and NIPPV are ways of supporting babies breathing in a less invasive way - the tubes are shorter and go only to the back of the nose and, therefore, cause less damage. NCPAP and NIPPV may be used after extubation to reduce the number of babies that need to have the endotracheal tube reinstituted. NCPAP provides steady pressure to the back of the nose which is transmitted to the lungs, helping the baby breath more comfortably. NIPPV provides the same support, but also adds some breaths from the ventilator. The three studies that have compared NCPAP and NIPPV each show that NIPPV reduces the need for the endotracheal tube to be reinstituted. Further studies are needed to make sure NIPPV is safe.

BACKGROUND

Preterm infants may experience difficulty with spontaneous, unassisted breathing for a variety of reasons including lung immaturity, chest wall instability, upper airway obstruction and poor central respiratory drive. Historically, the primary method of support for these infants has been endotracheal intubation and intermittent positive pressure ventilation. While this method is effective, it is accompanied by complications (upper airway damage, bronchopulmonary dysplasia, sepsis) and is associated with considerable economic cost. Minimising the duration of endotracheal intubation or avoiding it completely has been a goal of neonatal intensive care. Nasal continuous positive airway pressure (NCPAP) is a less invasive way of providing respiratory support to neonates at risk of,

or actually experiencing respiratory failure. A systematic review of trials comparing nasal continuous airway pressure (NCPAP) with treatment with oxyhood concluded that NCPAP begun immediately following a period of endotracheal intubation reduces the rate of adverse events (apnea, respiratory acidosis, and increased oxygen requirements) leading to reintubation (Davis 1999). In this systematic review, approximately a quarter of all preterm infants allocated to NCPAP failed extubation, therefore, the opportunity exists to further improve outcomes for infants thought to no longer require an endotracheal tube.

Adults and older children with acute or chronic ventilatory failure of various etiologies, including chronic obstructive pulmonary disease (Bott 1993), severe kyphoscoliosis (Ellis 1988) and pre-lung transplantation cystic fibrosis (Piper 1992) have been treated with intermittent positive pressure ventilation delivered via a nasal interface. Improvements in respiratory function have been described.

Nasal intermittent positive pressure ventilation (NIPPV) has been used in neonates for a variety of indications. 53% of Canadian tertiary care nurseries in the mid 1980s (Ryan 1989) reported using NIPPV. The physiological benefits of the technique have been evaluated. NIPPV has been shown to reduce asynchronous thoracoabdominal motion, perhaps as a result of reducing tube resistance and/or better stabilisation of the chest wall (Kiciman 1998). Its use improves tidal and minute volumes and decreases the inspiratory effort required by neonates compared with NCPAP (Moretti 1999). This technique has not been without problems in neonates; Garland 1985 reported an association between the use of ventilation via nasal prongs and an increased risk of gastrointestinal perforation. In the past, the lack of high quality evidence has led to variability in practice between neonatal intensive care units with respect to this potentially useful method of respiratory support.

OBJECTIVES

To determine the effect of management with nasal intermittent positive pressure ventilation (NIPPV) compared to continuous positive airway pressure (NCPAP) on the need for additional ventilatory support in preterm infants having their endotracheal tube removed following a period of intermittent positive pressure ventilation (IPPV).

In addition, we sought to compare the rates of endotracheal reintubation, gastric distension, gastrointestinal perforation, chronic lung disease, duration of hospitalisation and rates of apnea between the two groups.

A sensitivity analysis including only truly randomised trials was planned if any quasi-randomised trials were identified.

Subgroup analyses were planned to determine whether responses differed according to different methods of NIPPV delivery (synchronised or not, nasal or nasopharyngeal). Subgroup analysis was planned to determine whether the use of methylxanthines alters responses.

METHODS

Criteria for considering studies for this review

Types of studies

All randomised and quasi-randomised trials were included

Types of participants

Preterm infants (i.e. those born before 37 completed weeks gestation) being extubated following a period of endotracheal intubation

Types of interventions

Intermittent positive pressure ventilation administered via the nasal route either by short nasal prongs or nasopharyngeal tubes vs. nasal CPAP delivered by the same methods.

Types of outcome measures

Primary outcome

Respiratory failure defined by respiratory acidosis, increased oxygen requirement or apnea that is frequent or severe leading to additional ventilatory support during the week post extubation

Secondary outcomes

1. Endotracheal reintubation during the week post-extubation
2. Rates of abdominal distension requiring cessation of feeds
3. Rates of gastrointestinal perforation diagnosed radiologically or at operation
4. Rates of chronic lung disease defined as 1) requirement for supplemental oxygen at 28 days of life or 2) requirement for supplemental oxygen at 36 weeks postmenstrual age
5. Duration of hospitalisation
6. Rates of apnea and bradycardia expressed as events per hour

Search methods for identification of studies

See: Collaborative Review Group search strategy.

MEDLINE (1966 - December 18, 2007) was searched using the MeSH terms: Infant, Newborn (exp) and Positive-pressure respiration (exp). Other sources included the Cochrane Central Register of Controlled Trials (CENTRAL, The Cochrane Library, Issue 4, 2007), CINAHL using search terms: Infant newborn and intermittent positive pressure ventilation. Expert informants, previous

reviews including cross-references and conference and symposia proceedings were used.

Data collection and analysis

The standard method of the Cochrane Collaboration and its Neonatal Group were used to assess the methodological quality of the trials.

The three review authors independently assessed the quality of studies using the following criteria: blinding of randomisation, blinding of intervention, completeness of follow-up and blinding of outcome measurement. Additional information was sought from the authors when required. Data were extracted independently by the three review authors and then compared and differences resolved. Categorical data (proportion requiring reintubation) were analysed using relative risk, risk difference and number needed to treat. Continuous data (frequency of apneas) were analysed using weighted mean difference. The fixed effects model was used.

Subgroup analyses were planned to determine whether responses differed according to methods of NIPPV delivery and whether or not methylxanthines were used concurrently. Subgroup analyses based on characteristics of participants were planned: birth weight (e.g. infants < 1000 g) and corrected age at time of intervention (e.g. infants < 28 weeks).

RESULTS

Description of studies

See: Characteristics of included studies; Characteristics of excluded studies.

Three trials meeting the inclusion criteria of the review were identified - Barrington 2001; Friedlich 1999; Khalaf 2001. Details are included in the Characteristics of Included Studies table. Rescue NIPPV was permitted for infants failing NCPAP in all three studies but the primary outcome was analysed on an intention to treat basis. The criteria for offering rescue treatment appeared to be at the clinicians' discretion and the proportions offered rescue NIPPV varied between the three trials. Therefore, the outcome "endotracheal reintubation", although available for each of the trials, assumed a different meaning in each.

The inclusion criteria varied somewhat between trials, but all three enrolled very low birth weight (VLBW) infants, i.e. those infants at moderate risk of requiring endotracheal reintubation. In two trials (Khalaf 2001; Barrington 2001) the use of methylxanthines was mandatory and in the third (Friedlich 1999) it was extensively prescribed (86%). Infants were extubated from low levels of ventilator support (ventilator rates < 25 breaths per minute and oxygen concentrations <40%). The differences in these settings between the studies were small. An interesting variation in ventilatory strategies was noted between the centres: In spite of little variation seen in enrolment criteria, Khalaf 2001 and Barrington 2001 extubated their infants at a median age of less than one week, whereas infants in the Friedlich 1999 study were extubated at a median age of 18.5 and 21 days in the two groups.

NIPPV delivery was synchronised in all trials using the Infant Star ventilator with Star Synch abdominal capsule. Ventilator settings applied after extubation varied between studies. IMV rates varied between 10 and 25 per minute, and PIP from that used pre-extubation to 2 to 4 cm water above that used pre-extubation. The levels used in the NCPAP groups also varied between studies - Barrington 2001 set a level of 6 cm water and Friedlich 1999 and Khalaf 2001 set a range between 4 and 6 cm water. No attempt was made to match NIPPV and NCPAP groups with respect to mean airway pressure delivered. Devices used to deliver NCPAP/NIPPV also varied. Barrington 2001 used binasal, short Hudson Prongs, Friedlich 1999 used binasal, nasopharyngeal tubes and Khalaf 2001 used Argyle prongs. The primary outcome (the rate of extubation failure) was assessed over the 72 hours post-extubation by Barrington 2001 and Khalaf 2001 and over 48 hours by Friedlich 1999.

Risk of bias in included studies

Methodological quality was assessed using the criteria of the Neonatal Cochrane Review Group.

Blinding of randomisation: All three included trials met this criterion.

Blinding of intervention: This was not attempted by any study.

Complete followup: Achieved in all trials.

Blinding of outcome measurement: This was not attempted by any study.

Effects of interventions

After discussion between the three review authors, there was no disagreement regarding quality assessment and data extraction from the three identified trials.

NIPPV VS. NCPAP to prevent extubation failure (Comparison 1)

Primary Outcome:

Respiratory failure post-extubation (Outcome 1.1):

The three trials each showed a statistically significant benefit for infants extubated to NIPPV in terms of prevention of extubation failure criteria. The meta-analysis showed the effect was also clinically important [typical RR 0.21 (95% CI 0.10, 0.45), typical RD -0.32 (95% CI -0.45, -0.20)] with only 3 (95% CI 2, 5) infants needing to be treated with NIPPV to prevent one extubation failure. Although the total number of infants randomised was rela-

tively small (n = 159), the large treatment effect size and consistency of the findings of the three studies strengthened this conclusion. The test for heterogeneity was non-significant (I squared 0%).

Secondary Outcomes:

Endotracheal reintubation (Outcome 1.2):

Not all NCPAP infants reaching extubation failure criteria were reintubated since a varying proportion of infants in each trial were offered rescue therapy with NIPPV. The pooled estimate of rates of endotracheal reintubation favoured NIPPV [typical RR 0.39 (95% CI 0.16, 0.97), typical RD -0.11 (95% CI -0.21, -0.01), NNT 9 (95% CI 5, 83)].

Gastrointestinal side effects (Outcome 1.2, 1.4):

No infant in any of the three studies had an intestinal perforation. Friedlich 1999 and Barrington 2001 reported rates of feeding cessation and Khalaf 2001 provided unpublished data for this outcome. There was no significant difference between the groups [typical RR 1.76 (95% CI 0.77, 4.05), typical RD 0.07 (95% CI -0.03, 0.18).

Chronic lung disease (CLD) (Outcome 1.5):

A trend to lower rates of CLD in infants randomised to NIPPV was noted in the two trials reporting this outcome (Barrington 2001; Khalaf 2001). This did not reach statistical significance [typical RR 0.73 (95% CI 0.49, 1.07), typical RD -0.15 (95% CI -0.33, 0.03)].

Duration of hospitalisation (Outcome 1.6):

There were no differences in duration of hospitalisation. These results should be viewed with caution because the liberal use of rescue NIPPV for infants failing NCPAP within the first days of extubation makes differences in longer term outcomes, should they exist, more difficult to establish.

Rates of apnea (Outcome 1.7):

Barrington 2001 used continuous multi-channel recording to detect apneic events. There was a trend towards a reduction in numbers of apneic episodes per day in the NIPPV group, which did not reach statistical significance [WMD -3.1 (-7.9, 1.7)].

All three studies used synchronised NIPPV. Therefore, no subgroup analysis was performed to examine whether this is an important factor in successful delivery of NIPPV. Furthemore, almost all infants received methylxanthines prior to extubation so the planned subgroup analysis was not performed. Two trials used short binasal prongs (Barrington 2001; Khalaf 2001) and the other binasopharyngeal prongs (Friedlich 1999). Both were effective and the question of which is superior remains unanswered.

Comparisons of NIPPV with NCPAP in both studies are potentially confounded because of differences in mean airway pressure (MAP) between the groups. None of the authors present data on MAP in the NIPPV group, but the MAP may have been higher than the CPAP level in the other group. Differences in outcomes may simply be due to a higher mean airway pressure in the NIPPV group.

DISCUSSION

The three trials identified in this review have no major methodological limitations. Because of the nature of the interventions it has been impossible to blind caregivers and the possibility exists that bias may have arisen through uneven use of cointerventions. Potential confounders such as methylxanthine usage and weaning strategies have been dealt with by having management protocols in place, and the use of objective failure criteria in the extubation trials enhances confidence in their findings.

NIPPV is a potentially useful way of augmenting NCPAP. The relatively recent ability to synchronise the ventilator breaths with the infant's own respiratory cycle has led to renewed interest in this mode of ventilatory support. For the reasons outlined in the Background section it appears desirable to minimise the duration of endotracheal intubation of preterm infants, and the results of this review suggest that NIPPV may assist in achieving this aim by lowering the rate of respiratory failure after extubation. Infants being extubated following a period of endotracheal intubation have a reduced incidence of symptoms leading to reintubation, in particular respiratory acidosis and apnea. However, it is also apparent that, within the small population studied, infants "failing" NCPAP may be rescued by a course of NIPPV. Individual neonatal intensive care units may interpret these results differently. The provision of synchronised NIPPV requires a ventilator capable of delivering this mode of support. Less expensive methods of NCPAP delivery exist and issues of resource allocation may be important in some hospitals where synchronised NIPPV may be reserved for infants who "earn" it. Alternatively, well equipped units may elect to "prophylactically" use synchronised NIPPV to ensure stability of their infants.

AUTHORS' CONCLUSIONS

Implications for practice

NIPPV is a useful method of augmenting the beneficial effects of NCPAP in preterm infants. The use of NIPPV after extubation reduces the incidence of symptoms of extubation failure when compared with NCPAP. Within the limits of the small numbers of infants randomised to NIPPV there is a reassuring absence of the gastrointestinal side-effects that were reported in previous case series.

Implications for research

Future trials should enrol sufficient infants to detect differences in important outcomes such as chronic lung disease and gastrointestinal perforation. The impact of synchronisation of NIPPV on the technique's safety and efficacy should be established in future trials. Such trials may consider matching the MAP rather than

PEEP level in NIPPV infants to the CPAP level in the NCPAP group.

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* *Indicates the major publication for the study*

CHARACTERISTICS OF STUDIES

Characteristics of included studies *[ordered by study ID]*

Barrington 2001

Methods	Blinding of randomisation: Yes - sequentially numbered sealed opaque envelopes. Blinding of intervention: No Complete followup: Yes Blind outcome assessment: No
Participants	Included infants < 1250g birth weight (mean 831 +/- 193g) , <6 weeks of age (mean 7.6 +/- 9.7 days), requiring < 35% oxygen and <18 breaths per minute on synchronised intermittent mechanical ventilation. All infants loaded with aminophylline before extubation.
Interventions	Experimental group - synchronised NIPPV = nSIMV: R of 12 and PIP of 16, PEEP of 6, PIP increased to achieve measured pressure of at least 12. Used Grasby capsule, Infant Star ventilator and Hudson nasal prongs. Control: Nasal CPAP of 6.
Outcomes	Primary: failure of extubation by 72 hours because of either pCO2 >70, oxygen requirement of >70% or severe or recurrent apnea (defined). Secondary: rates of reintubation, abdominal distension, feeding intolerance and chronic lung disease.
Notes	Power calculation performed. 54 infants enrolled - 27 in each group. Most infants failing NCPAP tried on NIPPV before reintubation.

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Friedlich 1999

Methods	Blinding of randomisation: Yes - sealed randomisation cards. Blinding of intervention: No Complete follow up: Yes Blind outcome assessment: No
Participants	Included: infants with birthweight 500 -1500g (means 963+/- 57g and 944 +/- 43g) considered by attending ready for extubation (SIMV rate < 12, peak pressure <23, end expiratory pressure <6, oxygen requirement < 40%. Aminophylline not mandated but given in ~ 85% of infants. Extubated at 26.3 +/- 6.1 and 19.9 +/-3.8 days of life. Excluded: infants with sepsis, necrotising enterocolitis, symptomatic PDA, congenital anomalies.

Friedlich 1999 (*Continued*)

Interventions	Experimental group - nasopharyngeal 3 Fr gauge tube, Infant Star ventilator, synchronised NIPPV = nSIMV with rate of 10, PIP = that before extubation, PEEP 4-6, IT = 0.6. Control: nasopharyngeal CPAP to desired level of attending.
Outcomes	Primary: failure of extubation by 48 hours because either pH < 7.25, pCO2 increased by 25%, oxygen requirement greater than 60%, SIMV rate > 20 (in NIPPV group), PIP > 26 or PEEP > 8 in NIPPV group, apnea requiring bag and mask ventilation. Secondary: endotracheal reintubation, abdominal distension, perforation or NEC, feeding delay (not defined) and nasal bleeding.
Notes	Power calculation performed. Study closed early after interim analysis (stopping rule not specified). 41 infants enrolled - 22 NIPPV and 19 NCPAP. Most infants failing NCPAP tried on NIPPV before reintubation.

Risk of bias

Item	Authors' judgement	Description
Allocation concealment?	Yes	A - Adequate

Khalaf 2001

Methods	Blinding of randomisation: Yes - sealed envelopes Blinding of intervention: No Complete follow-up: Yes Blinding of outcome assessment: No
Participants	Included: infants with gestational age (GA) < 34 weeks with respiratory distress syndrome ventilated using an endotracheal tube. Mean birthweights 1088g and 1032g and mean GAs of 28 weeks. Ventilator settings PIP<or=16 cm water, PEEP<or=5, R 15-25/minute and <35% oxygen. All had a therapeutic blood level of aminophylline and hematocrit > 40%.
Interventions	Experimental group - synchronised NIPPV via Argyle prongs, Infant Star ventilator at PEEP level less than or equal to 5 cm water, rate of 15 to 25 per minute and PIP set 2 to 4 cm water above that used pre-extubation. Gas flow set at 8-10 l/minute in both groups. Conrol group had NCPAP delivered by Argyle prongs from a Bear Cub or Infant Star ventilator at level of 4 to 6 cm water.
Outcomes	Primary: failure of extubation by 72 hours because pH<7.25 or pCO2>60 mm Hg, single episode of severe apnea requiring bag and mask ventilation or frequent apnea or desaturations (defined). Secondary outcomes included chronic lung disease defined as supplemental oxygen requirement at 36 weeks corrected age, days of ventilation and hospitalisation. Data on rates of feeding intolerance provided by authors.
Notes	Power calculation performed. 64 infants enrolled - 34 NIPPV and 30 NCPAP. Two infants failing NCPAP tried on NIPPV (successfully)before reintubation. For the outcome "abdominal distension causing cessation of feeds" the denominators are the numbers offered enteral feeds during the 72 hour study period i.e. 21(NIPPV) and 20 (NCPAP).

Khalaf 2001 (*Continued*)

Risk of bias		
Item	**Authors' judgement**	**Description**
Allocation concealment?	Yes	A - Adequate

PIP = peak inspiratory pressure (cm of water), PEEP = positive end expiratory pressure (cm of water), R = ventilator rate (breaths per minute), CPAP = continuous positive airway pressure (cm of water), IT = inspiratory time (seconds), nSIMV = nasal synchronised intermittent mechanical ventilation, NIPPV = nasal intermittent positive pressure ventilation, NEC = necrotising enterocolitis, IVH = intraventricular hemorrhage

Characteristics of excluded studies *[ordered by study ID]*

Ali 2007	Ali compared a form of NIPPV (non-invasive pressure support ventilation with NCPAP in a randomised cross-over study. The study compared short-term physiological outcomes (tidal volume, breathing effort etc.). It was excluded because it did not report any of the clinical outcomes listed in the inclusion criteria of this review.
Bhandari 2007	Randomised trial of NIPPV vs conventional ventilation for management of RDS, i.e. different groups compared for a different indication.
Bisceglia 2007	Randomised trial of NIPPV vs NCPAP for moderate respiratory distress syndrome, i.e. different inclusion criteria.
Moretti 1999	Randomised cross-over trial. Each infant (n=11, mean BW=1141g) received NIPPV and NCPAP in random order for a period of 1 hour. Outcomes were respiratory rates and pulmonary function tests, i.e. not those outcome criteria specified in the protocol

DATA AND ANALYSES

Comparison 1. NIPPV vs NCPAP to prevent extubation failure

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 Respiratory failure post-extubation	3	159	Risk Ratio (M-H, Fixed, 95% CI)	0.21 [0.10, 0.45]
1.1 Short (nasal) prongs	2	118	Risk Ratio (M-H, Fixed, 95% CI)	0.24 [0.11, 0.53]
1.2 Long (nasopharyngeal) prongs	1	41	Risk Ratio (M-H, Fixed, 95% CI)	0.12 [0.02, 0.91]
2 Endotracheal reintubation	3	159	Risk Ratio (M-H, Fixed, 95% CI)	0.39 [0.16, 0.97]
3 Abdominal distension causing cessation of feeds	3	136	Risk Ratio (M-H, Fixed, 95% CI)	1.76 [0.77, 4.05]
4 Gastrointestinal perforation	3	159	Risk Ratio (M-H, Fixed, 95% CI)	Not estimable
5 Chronic lung disease (oxygen supplementation at 36 weeks)	2	118	Risk Ratio (M-H, Fixed, 95% CI)	0.73 [0.49, 1.07]
6 Duration of hospitalisation (days)	2	118	Mean Difference (IV, Fixed, 95% CI)	-5.48 [-16.76, 5.79]
7 Rates of apnea (episodes/24 hours)	1	54	Mean Difference (IV, Fixed, 95% CI)	-3.10 [-7.92, 1.72]

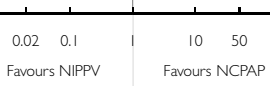
Analysis 1.1. Comparison 1 NIPPV vs NCPAP to prevent extubation failure, Outcome 1 Respiratory failure post-extubation.

Review: Nasal intermittent positive pressure ventilation (NIPPV) versus nasal continuous positive airway pressure (NCPAP) for preterm neonates after extubation

Comparison: 1 NIPPV vs NCPAP to prevent extubation failure

Outcome: 1 Respiratory failure post-extubation

Study or subgroup	NIPPV n/N	NCPAP n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
1 Short (nasal) prongs					
Barrington 2001	4/27	12/27		37.2 %	0.33 [0.12, 0.90]
Khalaf 2001	2/34	12/30		39.5 %	0.15 [0.04, 0.60]
Subtotal (95% CI)	**61**	**57**		**76.7 %**	**0.24 [0.11, 0.53]**
Total events: 6 (NIPPV), 24 (NCPAP)					
Heterogeneity: Chi² = 0.88, df = 1 (P = 0.35); I² =0.0%					
Test for overall effect: Z = 3.48 (P = 0.00051)					
2 Long (nasopharyngeal) prongs					
Friedlich 1999	1/22	7/19		23.3 %	0.12 [0.02, 0.91]
Subtotal (95% CI)	**22**	**19**		**23.3 %**	**0.12 [0.02, 0.91]**
Total events: 1 (NIPPV), 7 (NCPAP)					
Heterogeneity: not applicable					
Test for overall effect: Z = 2.05 (P = 0.041)					
Total (95% CI)	**83**	**76**		**100.0 %**	**0.21 [0.10, 0.45]**
Total events: 7 (NIPPV), 31 (NCPAP)					
Heterogeneity: Chi² = 1.33, df = 2 (P = 0.51); I² =0.0%					
Test for overall effect: Z = 4.07 (P = 0.000048)					



Analysis 1.2. Comparison 1 NIPPV vs NCPAP to prevent extubation failure, Outcome 2 Endotracheal reintubation.

Review: Nasal intermittent positive pressure ventilation (NIPPV) versus nasal continuous positive airway pressure (NCPAP) for preterm neonates after extubation

Comparison: 1 NIPPV vs NCPAP to prevent extubation failure

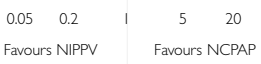
Outcome: 2 Endotracheal reintubation

Study or subgroup	NIPPV n/N	NCPAP n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Barrington 2001	3/27	3/27		20.4 %	1.00 [0.22, 4.52]
Friedlich 1999	1/22	1/19		7.3 %	0.86 [0.06, 12.89]
Khalaf 2001	2/34	10/30		72.3 %	0.18 [0.04, 0.74]
Total (95% CI)	**83**	**76**		**100.0 %**	**0.39 [0.16, 0.97]**

Total events: 6 (NIPPV), 14 (NCPAP)

Heterogeneity: Chi^2 = 2.99, df = 2 (P = 0.22); I^2 =33%

Test for overall effect: Z = 2.03 (P = 0.043)



Analysis 1.3. Comparison 1 NIPPV vs NCPAP to prevent extubation failure, Outcome 3 Abdominal distension causing cessation of feeds.

Review: Nasal intermittent positive pressure ventilation (NIPPV) versus nasal continuous positive airway pressure (NCPAP) for preterm neonates after extubation

Comparison: 1 NIPPV vs NCPAP to prevent extubation failure

Outcome: 3 Abdominal distension causing cessation of feeds

Study or subgroup	NIPPV n/N	NCPAP n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Barrington 2001	10/27	6/27		1.67 [0.71, 3.94]
Friedlich 1999	0/22	0/19		0.0 [0.0, 0.0]
Khalaf 2001	1/21	0/20		2.86 [0.12, 66.44]
Total (95% CI)	**70**	**66**		**1.76 [0.77, 4.05]**

Total events: 11 (NIPPV), 6 (NCPAP)

Heterogeneity: Chi^2 = 0.11, df = 1 (P = 0.74); I^2 =0.0%

Test for overall effect: Z = 1.33 (P = 0.18)

Analysis 1.4. Comparison 1 NIPPV vs NCPAP to prevent extubation failure, Outcome 4 Gastrointestinal perforation.

Review: Nasal intermittent positive pressure ventilation (NIPPV) versus nasal continuous positive airway pressure (NCPAP) for preterm neonates after extubation

Comparison: 1 NIPPV vs NCPAP to prevent extubation failure

Outcome: 4 Gastrointestinal perforation

Study or subgroup	NIPPV n/N	NCPAP n/N	Risk Ratio M-H,Fixed,95% CI	Risk Ratio M-H,Fixed,95% CI
Barrington 2001	0/27	0/27		0.0 [0.0, 0.0]
Friedlich 1999	0/22	0/19		0.0 [0.0, 0.0]
Khalaf 2001	0/34	0/30		0.0 [0.0, 0.0]
Total (95% CI)	**83**	**76**		**0.0 [0.0, 0.0]**

Total events: 0 (NIPPV), 0 (NCPAP)

Heterogeneity: $Chi^2 = 0.0$, df = 0 (P<0.00001); $I^2 = 0.0\%$

Test for overall effect: Z = 0.0 (P < 0.00001)

Analysis 1.5. Comparison 1 NIPPV vs NCPAP to prevent extubation failure, Outcome 5 Chronic lung disease (oxygen supplementation at 36 weeks).

Review: Nasal intermittent positive pressure ventilation (NIPPV) versus nasal continuous positive airway pressure (NCPAP) for preterm neonates after extubation

Comparison: 1 NIPPV vs NCPAP to prevent extubation failure

Outcome: 5 Chronic lung disease (oxygen supplementation at 36 weeks)

Study or subgroup	NIPPV n/N	NCPAP n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Barrington 2001	12/27	15/27		46.9 %	0.80 [0.47, 1.37]
Khalaf 2001	12/34	16/30		53.1 %	0.66 [0.38, 1.16]
Total (95% CI)	**61**	**57**		**100.0 %**	**0.73 [0.49, 1.07]**

Total events: 24 (NIPPV), 31 (NCPAP)

Heterogeneity: $Chi^2 = 0.23$, df = 1 (P = 0.63); $I^2 = 0.0\%$

Test for overall effect: Z = 1.60 (P = 0.11)

Analysis 1.6. Comparison 1 NIPPV vs NCPAP to prevent extubation failure, Outcome 6 Duration of hospitalisation (days).

Review: Nasal intermittent positive pressure ventilation (NIPPV) versus nasal continuous positive airway pressure (NCPAP) for preterm neonates after extubation

Comparison: 1 NIPPV vs NCPAP to prevent extubation failure

Outcome: 6 Duration of hospitalisation (days)

Study or subgroup	NIPPV N	Mean(SD)	NCPAP N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Barrington 2001	27	86 (23)	27	92 (26)		74.1 %	-6.00 [-19.09, 7.09]
Khalaf 2001	34	72 (46.65)	30	76 (43.82)		25.9 %	-4.00 [-26.18, 18.18]
Total (95% CI)	**61**		**57**			**100.0 %**	**-5.48 [-16.76, 5.79]**

Heterogeneity: Chi^2 = 0.02, df = 1 (P = 0.88); I^2 =0.0%

Test for overall effect: Z = 0.95 (P = 0.34)

Analysis 1.7. Comparison 1 NIPPV vs NCPAP to prevent extubation failure, Outcome 7 Rates of apnea (episodes/24 hours).

Review: Nasal intermittent positive pressure ventilation (NIPPV) versus nasal continuous positive airway pressure (NCPAP) for preterm neonates after extubation

Comparison: 1 NIPPV vs NCPAP to prevent extubation failure

Outcome: 7 Rates of apnea (episodes/24 hours)

Study or subgroup	NIPPV N	Mean(SD)	NCPAP N	Mean(SD)	Mean Difference IV,Fixed,95% CI	Weight	Mean Difference IV,Fixed,95% CI
Barrington 2001	27	5.1 (4.4)	27	8.2 (12)		100.0 %	-3.10 [-7.92, 1.72]
Total (95% CI)	**27**		**27**			**100.0 %**	**-3.10 [-7.92, 1.72]**

Heterogeneity: not applicable

Test for overall effect: Z = 1.26 (P = 0.21)

WHAT'S NEW

Last assessed as up-to-date: 22 June 2008.

13 February 2009	Amended	Contact details updated

HISTORY

Protocol first published: Issue 4, 1999

Review first published: Issue 3, 2001

23 June 2008	New search has been performed	This review updates the previous version of "Nasal intermittent positive pressure ventilation (NIPPV) versus nasal continuous positive airway pressure NCPAP) for preterm infants after extubation " last updated in The Cochrane Library, Issue 3, 2003 (Davis 2003). A repeat literature search found no new trials eligible for inclusion. There have been no substantive changes to the review. One potentially eligible trial (Yllescas, 2004) was presented at APS and may be included in a future update.
14 April 2008	Amended	Converted to new review format.
14 April 2003	New search has been performed	A repeat literature search showed no new trials eligible for inclusion and there have been no substantive changes to the review.
9 May 2001	New citation required and conclusions have changed	New review

CONTRIBUTIONS OF AUTHORS

PGD and BL prepared the protocol for this review. AGD provided additional material for the Background. All three review authors performed a literature search, made independent quality assessments and extracted data before comparing results and resolving differences.

DECLARATIONS OF INTEREST

None

SOURCES OF SUPPORT

Internal sources

- Royal Women's Hospital, Melbourne, Australia.
- Murdoch Children's Research Institute, Melbourne, Australia.
- University of Melbourne, Australia.
- Royal Hobart Hospital, Australia.
- University of Tasmania, Australia.

External sources

- National Health and Medical Research Council, Australia.

INDEX TERMS

Medical Subject Headings (MeSH)

*Infant, Premature; Infant, Newborn; Intermittent Positive-Pressure Ventilation; Intubation, Intratracheal; Positive-Pressure Respiration [*methods]; Randomized Controlled Trials as Topic

MeSH check words

Humans