Nasal intermittent positive-pressure ventilation vs nasal continuous positive airway pressure for preterm infants with respiratory distress syndrome: a systematic review and meta-analysis

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CRD summary
Nasal intermittent positive-pressure ventilation reduced the need for intubation and invasive mechanical ventilation within the first 72 hours of life in preterm infants with respiratory distress syndrome compared with continuous positive airway pressure. The conclusions and recommendations for research of this well-conducted review seem reliable but are based on a small amount of evidence.

Authors' objectives
To compare nasal intermittent positive-pressure ventilation (NIPPV) with nasal continuous positive airway pressure (NCPAP) for reducing the need for invasive ventilation within the first 72 hours of life in preterm infants with respiratory distress syndrome.

Searching
MEDLINE, EMBASE, CINAHL, Cochrane Central Register of Controlled Trials (CENTRAL) and ClinicalTrials.gov were searched for articles published between January 1990 and April 2011. There were no language restrictions. Abstracts from meetings of Pediatric Academic Societies (2000 to 2011) were searched. Medical Subject Headings (MeSH) terms used in the search were reported.

Study selection
Randomised controlled trials that compared noninvasive ventilation strategies (NIPPV and NCPAP) in preterm infants with respiratory distress syndrome who needed intubation and mechanical ventilation were eligible for inclusion. The primary outcome was need for intubation and mechanical ventilation in the first 72 hours of life. Secondary outcomes were bronchopulmonary dysplasia (need for supplemental oxygen at 36 weeks postmenstrual age), necrotising enterocolitis, pneumothorax, intraventricular haemorrhage of any grade, time to full feeds (130 to 150mL/kg/day) and duration of hospital stay.

Gestational ages in the included studies were 26 to 34 weeks, 28 to 34 weeks plus a birthweight of 750g or more or less than 35 weeks. Two studies evaluated ventilator-derived NCPAP and one evaluated bubble NCPAP.

Studies were independently reviewed for eligibility. The number of reviewers involved was unclear.

Assessment of study quality
Trial quality was assessed using Cochrane Collaboration guidelines and covered adequate sequence generation, allocation concealment, blinding of investigators and outcome assessors, completeness of outcome data, selective reporting and other bias.

Study quality assessment was performed independently. The number of reviewers was unclear.

Data extraction
Risk ratios (RR) were calculated for dichotomous outcomes and mean differences for continuous outcomes, both with 95% confidence intervals (CI).

Data were extracted by two reviewers independently. Disagreements were resolved by three reviewers.

Methods of synthesis
Results were pooled using fixed-effect meta-analysis or random-effects models where there was considerable heterogeneity was present. Statistical heterogeneity was assessed using $X^2$ and $I^2$. $I^2$ approximating 25%, 50% and 75% was considered low, medium and high heterogeneity.
Results of the review
Three trials (360 participants) were included. All were considered to have low risk of bias for all items in the risk of bias assessment.

NIPPV significantly reduced the need for invasive ventilation within the first 72 hours of life compared with NCPAP (RR 0.60, 95% CI 0.43 to 0.83; three trials). No heterogeneity was found ($I^2=1\%$). Results for the two trials where infants received surfactant by the INSURE (intubate-surfactant-extubate) approach were combined and there was no significant difference between the ventilation methods.

No significant differences between ventilation methods were found for bronchopulmonary dysplasia, the composite outcome of death and bronchopulmonary disease, pneumothorax, intraventricular haemorrhage, necrotising enterocolitis, time to full feeds and duration of hospital stay; moderate heterogeneity was observed for bronchopulmonary dysplasia and duration of hospital stay. No gastric perforation was reported amongst the 180 infants in the NIPPV groups from all three trials.

Authors’ conclusions
NIPPV compared with NCPAP showed benefits for preterm infants with respiratory distress syndrome with a significant reduction in need for intubation and invasive mechanical ventilation within the first 72 hours of life.

CRD commentary
This review had a clear research question and specified inclusion criteria in enough detail to enable independent replication. Several relevant databases as well as trials registers and abstracts of conferences in the field were searched. There were no restrictions by language. It was reported that study eligibility and quality were performed independently but the number of reviewers involved was unclear; data were extracted by two reviewers independently to reduce bias or errors.

The statistical analysis methods were appropriate. Trial quality was assessed and fully reported. Only three trials were included and all were considered low risk of bias.

The conclusions and recommendations for research of this well-conducted review seem reliable but are based on a small amount of evidence.

Implications of the review for practice and research
Practice: The authors did not state any recommendations for practice.

Research: The authors stated that larger trials of the most vulnerable preterm infants with longer intervention periods were needed to compare NIPPV with nasal continuous positive airway pressure. Trials are also needed to evaluate whether NCPAP reduced bronchopulmonary dysplasia and other comorbidities.

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