

Elective High-Frequency Oscillatory Ventilation versus Conventional Ventilation for Acute Pulmonary Dysfunction in Preterm Infants

Cochrane Abstract

Background: Respiratory failure due to lung immaturity is a major cause of mortality in preterm infants. Although the use of intermittent positive pressure ventilation in neonates with respiratory failure saves lives, its use is associated with lung injury and chronic lung disease (CLD). A newer form of ventilation called high-frequency oscillatory ventilation (HFOV) has been shown to result in less lung injury in experimental studies. **Objectives:** The objective of this review is to determine the effect of the elective use of HFOV as compared to conventional ventilation (CV) on the incidence of CLD, mortality and other complications associated with prematurity and assisted ventilation in preterm infants who are mechanically ventilated for respiratory distress syndrome (RDS). **Search Methods:** Searches were made of the Oxford Database of Perinatal Trials, MEDLINE, EMBASE, previous reviews including cross-references, abstracts, conferences and symposia proceedings, expert informants, journal hand searching by the Cochrane Collaboration, mainly in the English language. The search was updated in January 2009. **Selection Criteria:** Randomized controlled trials comparing HFOV and CV in preterm or low birth weight infants with pulmonary dysfunction, mainly due to RDS, who required assisted ventilation. Randomization and commencement of treatment needed to be as soon as possible after the start of

CV and usually in the first 12 h of life. **Data Collection and Analysis:** The methodological quality of each trial was independently reviewed by the various authors. The standard effect measures are relative risk (RR) and risk difference (RD). From 1/RD the number needed to treat to produce one outcome were calculated. For all measures of effect, 95% confidence intervals were used. In subgroup analyses the 99% CIs are also given for summary RRs in the text. Meta-analysis was performed using a fixed effect model. Where heterogeneity was over 50%, the random effects RR is also given. **Main Results:** Seventeen eligible studies of 3,652 infants were included. Meta-analysis comparing HFOV with CV revealed no evidence of effect on mortality at 28–30 days of age or at approximately term equivalent age. These results were consistent across studies and in subgroup analyses. The effect of HFOV on CLD in survivors at term equivalent gestational age was inconsistent across studies and the reduction was of borderline significance overall. The effect was similar in trials with a high lung volume strategy for HFOV targeting at very low FiO_2 and trials with a high lung volume strategy with somewhat higher or unspecified target FiO_2 . Subgroups of trials showed a significant reduction in CLD with HFOV when no surfactant was used, when piston oscillators were used for HFOV, when lung protective strategies for CV were not used, when randomization occurred at two to six hours of age, and when inspiratory:expiratory ratio of 1:2 was used for

HFOV. In the meta-analysis of all trials, pulmonary air leaks occurred more frequently in the HFOV group. In some studies, short-term neurological morbidity with HFOV was found, but this effect was not statistically significant overall. The subgroup of two trials not using a high-volume strategy with HFOV found increased rates of grade 3 or 4 intraventricular hemorrhage and of periventricular leukomalacia. An adverse effect of HFOV on long-term neurodevelopment was found in one large trial but not in the five other trials that reported this outcome. The rate of retinopathy of prematurity is reduced overall in the HFOV group.

Reviewers' Conclusions

There is no clear evidence that elective HFOV offers important advantages over CV when used as the initial ventilation strategy to treat preterm infants with acute pulmonary dysfunction. There may be a small reduction in the rate of CLD with HFOV use, but the evidence is weakened by the inconsistency of this effect across trials and the overall borderline significance. Future trials on elective HFOV should target those infants who are at most risk of CLD (extremely preterm infants), compare different strategies for generating HFOV and CV, and report important long-term neurodevelopmental outcomes.

Cools F, Offringa M, Askie LM: Elective high-frequency oscillatory ventilation versus conventional ventilation for acute pulmonary dysfunction in preterm infants. *Cochrane Database of Systematic Reviews* 2009, Issue 3. Art. No.: CD000104. DOI: [10.1002/14651858.CD000104.pub3](https://doi.org/10.1002/14651858.CD000104.pub3).

Commentary

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High-frequency oscillatory ventilation (HFOV) is a way of providing artificial ventilation of the lungs that theoretically may produce less injury to the lungs and therefore reduce the rate of chronic lung disease. Cools and colleagues have updated the Cochrane Review of 'Elective high-frequency oscillatory ventilation versus conventional ventilation for acute pulmonary dysfunction in preterm infants'. Seventeen trials involving over 3,652 infants are included. The updated meta-analysis comparing HFOV with conventional ventilation in infants with early respiratory distress revealed few clinical

differences. The results demonstrated inconsistent effects regarding clinical improvement for important outcomes, including chronic lung disease and death (fig. 1).

Like many study level meta-analyses, this analysis has been criticized because it is hard to tease out the effect of specific patient characteristics, differences in ventilators and differences in ventilator strategy. To answer this question, Cools et al. [1] have published a separate individual patient meta-analysis regarding elective high-frequency oscillatory versus conventional ventilation in preterm infants. In this study, over 3,000 participants from ten of the randomized, controlled trials had individual patient data collected. For infants ventilated with high-frequency oscillation, the relative risk of death or bronchopulmonary dysplasia at 36 weeks' postmenstrual age was 0.95 (95% CI 0.88–1.03) and the risk of death or severe adverse neurological events was 1.0 (95% CI 0.88–1.13). In the individual patient data meta-analysis, no subgroup of infants (e.g. gestational age, birth weight for gestation, initial lung disease severity or exposure to antenatal steroids) benefited more or less from HFOV. Ventilator type or ventilator strategy did not change the overall treatment effect.

Despite limited evidence for efficacy, almost 1 out of every 5 very low birth weight infants receives HFOV at some point in their NICU course [2]. It could be argued that there are no disadvantages of this approach but, as neonatal care spreads worldwide, there seems to be little role for this more expensive and complicated approach to ventilator management.

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References

- 1 Cools F, Askie LM, Offringa M, Asselin JM, Calvert SA, Courtney SE, Dani C, Durand DJ, Gerstmann DR, Henderson-Smart DJ, Marlow N, Peacock JL, Pillow JJ, Soll RF, Thome UH, Truffert P, Schreiber MD, Van Reempts P, Vendettuoli V, Vento G, PreVILIG Collaboration: Elective high-frequency oscillatory versus conventional ventilation in preterm infants: a systematic review and meta-analysis of individual patients' data. *Lancet* 2010;375:2082–2091.
- 2 Vermont Oxford Database 2010. <http://www.vtoxford.org/>.

(For figure 1 see next page.)

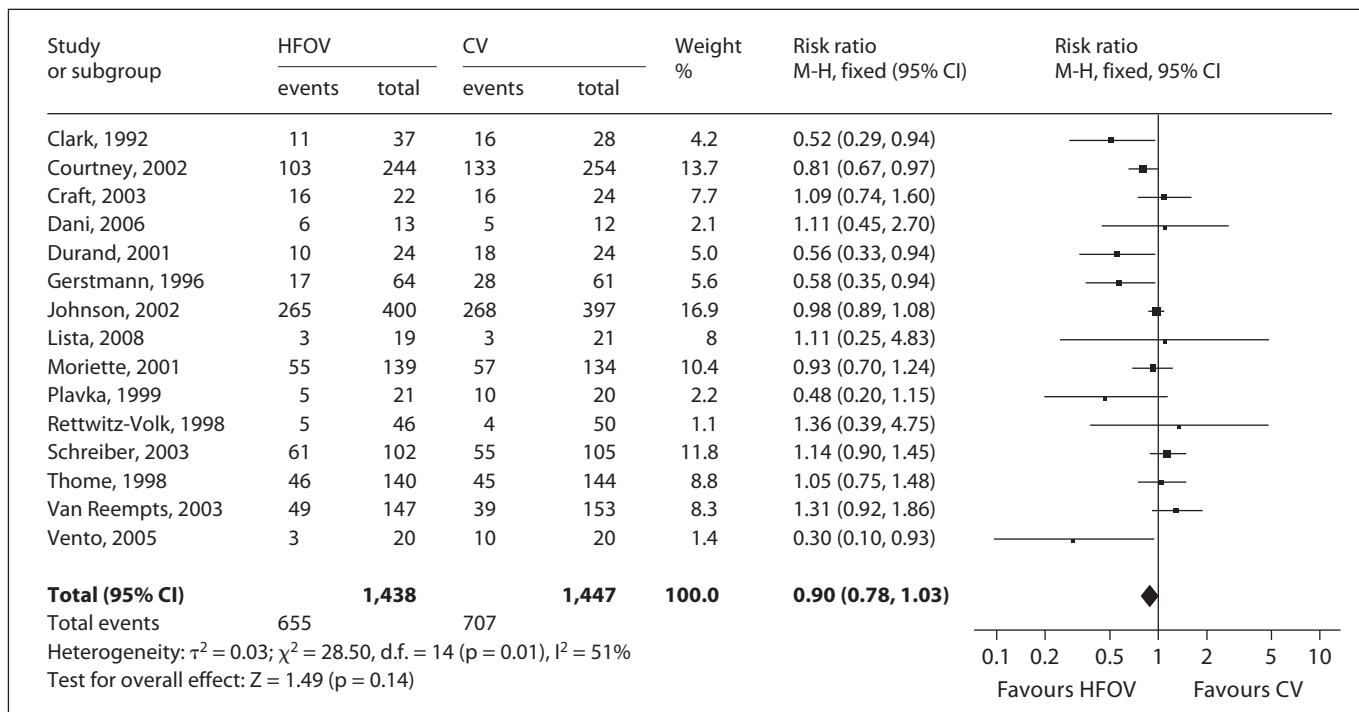


Fig. 1. Effect of elective HFOV compared to conventional mechanical ventilation on death or chronic lung disease at 36–37 weeks' postmenstrual age or discharge.