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

Yahya Al Ethawi
Women's Hospital, Health Sciences Center, Winnipeg, R3A 0L8, Manitoba, Canada. E-mail: yalethawi@hsc.mb.ca

STUDY QUESTION

Does elective use of high-frequency oscillatory ventilation (HFOV) as compared to conventional ventilation (CV) affect the incidence of chronic lung disease (CLD), mortality and other complications associated with prematurity and assisted ventilation in preterm infants who are mechanically ventilated for respiratory distress syndrome (RDS)?

METHODS

Eligibility

All randomized controlled or quasi-randomized trials comparing HFOV and CV in preterm or low birth weight infants with pulmonary dysfunction, mainly due to RDS, who required assisted ventilation were enrolled.

Types of interventions

Elective HFOV versus CV.

Inclusion

All elective trials: When randomization was accomplished early in the course of RDS soon after mechanical ventilation was begun. Such trials were classified as 'elective'.

Exclusion

All rescue trials, when patients were randomized after failure to adequately ventilate on CV or when complications of CV developed or were likely to develop.

Outcomes from trials were not eligible if there was a 20% or greater rate of missing or unreported data.

Outcomes

Primary

1. Mortality at 28 to 30 days and at term equivalent age
2. Chronic lung disease:
   - Oxygen dependency at 28 to 30 days (with and without chest x-ray changes)
   - Oxygen dependency or use of assisted ventilation at 36-37 weeks postmenstrual age (PMA) or discharge
3. Death or chronic lung disease

Secondary

1. Failure of allocated treatment to maintain gas exchange, leading to cross over to alternate treatment
2. Pulmonary air leak syndromes-all [including pulmonary interstitial emphysema (PIE) and gross extra-pulmonary air leak (such as pneumothorax)]
3. Intraventricular haemorrhage (IVH); all grades, grades 3 (ventricles distended with blood) or 4 (parenchymal involvement)
4. Periventricularleukomalacia (PVL)
5. Retinopathy of prematurity (ROP); grade 2 or more
6. Use of hospital resources (length of hospital stay, duration of IPPV)
7. Long-term growth and neurodevelopment

Search

Search was conducted using MeSH headings 'high-frequency ventilation' and 'infant, preterm' from 1983 to January 2009. Previous reviews including cross references, abstracts, conferences and symposia proceedings, expert informants, journal hand searching by the Cochrane Collaboration, mainly in the English language.

Search engines

1. Oxford Database of Perinatal Trials.
2. Cochrane Controlled Trials Register (CENTRAL).
3. The Cochrane Library Issue 4, 2008.
4. MEDLINE and EMBASE.

Expert informant's search in the Japanese language was made by Prof. Y. Ogawa in 1996. Abstracts of the annual meetings of Society for Pediatric Research (1996 to 2009 inclusive) were also searched.

Data collection

The standard methods of the Cochrane Collaboration and the Cochrane Neonatal Review Group (CNRG) were used to evaluate the methodological quality of each trial. Trials were reviewed independently by each author for eligibility. Data were extracted separately by each author, and then compared and any differences resolved.

Results for outcomes requiring survival to a given age are reported with survivors as the denominator (IPPV, CLD). Survival was used, as the denominator for ROP, where the number examined was not given.

The standard method of the CNRG was used to analyze the data. Treatment effects were expressed using relative risk (RR) and risk difference (RD). From 1/RD the number needed to treat (NNT) to produce one outcome was calculated. For each measure the 95% confidence intervals (CI) are routinely given. In subgroup analyses, the 99% CIs are also given for summary RRs in the text.

Meta-analysis was performed using a fixed effects model. Where heterogeneity was over 50%, the random effect RR is also given.

Population

All preterm or low birth weight infants; with pulmonary dysfunction, mainly due to RDS, who required intermittent positive pressure ventilation (IPPV).

RESULTS

Seventeen eligible studies of 3652 infants were included. Meta-analysis comparing HFOV with CV revealed no evidence of effect on mortality at 28 to 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 2 to 6 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 IVH and of PVL. 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.

CONCLUSION

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 neuro-developmental outcomes.

COMMENTARY

This evidence is supporting most of clinical human studies' conclusions that there are no substantial advantages or harms of elective HFOV (started early in the course of RDS or at the most beginning of ventilation) compared to CV especially when the lung protection strategy is used. The existing evidence to support the routine use of elective HFOV is week.

Abstracted from

Cools F, Henderson-Smart DJ, Offringa M, Askie LM. Elective high frequency oscillatory ventilation versus conventionalventilation for acute pulmonary dysfunction in preterm infants. Cochrane Database of Systematic Reviews 2009, Issue 3. Art. No.:
CD000104. DOI: 10.1002/14651858.CD000104.pub3.