Treatment

High frequency oscillatory ventilation was not more effective than conventional ventilation in preterm infants


QUESTION: In preterm infants who are 23–28 weeks gestational age, does high frequency oscillatory ventilation (HFOV) reduce death and chronic lung disease when compared with conventional ventilation (CV)?

Design
Randomised (unclear allocation concealment), unblinded, controlled trial with 8–13 weeks of follow up for the primary outcome.

Setting
25 centres: 22 in the UK and 1 each in Australia, Ireland, and Singapore.

Patients
870 infants were randomised before or just after delivery, 804 surviving infants who required endotracheal intubation from birth and ongoing intensive care were included. Exclusion criteria were transfer to another hospital for intensive care shortly after birth or major congenital abnormality, 797 infants (92%) (mean gestational age 26.5 wks, 54% boys) were included in the analysis.

Intervention
After stratification for gestational age and centre, infants were allocated to HFOV (n=400) or CV (n=397) within 1 hour of birth. HFOV was given by 1 of 3 high frequency oscillator models. Ventilation began at a mean airway pressure of 6–8 cm of water and a frequency of 10 Hz; the amplitude was increased until the infant’s chest was seen to be “bouncing”. CV was given by a time cycled, pressure limited ventilator, starting at a rate of 60 breaths per minute and an inspiratory time of 0.4 seconds. Settings were subsequently adjusted to maintain a partial pressure of oxygen of 49–75 mm Hg and a partial pressure of carbon dioxide of 34–53 mm Hg.

Main outcome measure
Composite endpoint of death or chronic lung disease (defined as dependence on supplemental oxygen) at 36 weeks gestational age.

Main results
Analysis was by intention to treat. HFOV did not differ from CV for the composite endpoint of death or chronic lung disease, death, or chronic lung disease (table).

Conclusion
In preterm infants who were 23–28 weeks gestational age, high frequency oscillatory ventilation did not reduce combined death and chronic lung disease more than conventional ventilation.

### TABLE: Outcomes at 36 weeks gestational age

<table>
<thead>
<tr>
<th>Outcome</th>
<th>HFOV</th>
<th>CV</th>
<th>RRR (95% CI)</th>
<th>NNT</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death or chronic lung disease</td>
<td>66%</td>
<td>68%</td>
<td>1.9% (0.2 to 11)</td>
<td>Not significant</td>
</tr>
<tr>
<td>Death</td>
<td>25%</td>
<td>26%</td>
<td>5.5% (0.2 to 25)</td>
<td>Not significant</td>
</tr>
<tr>
<td>Chronic lung disease</td>
<td>41.3%</td>
<td>41.0%</td>
<td>0.5% (0.15 to 19)</td>
<td>Not significant</td>
</tr>
</tbody>
</table>

*Abbreviations defined in glossary; RRR, RRI, NNT, NNH, and CI calculated from data in article.

COMMENTARY

CV delivers relatively large tidal volumes that can injure neonates’ lungs. HFOV uses rapid, small tidal volumes to avoid the large changes in lung volume. A systematic review of 6 randomised controlled trials (RCTs) comparing HFOV with CV showed that HFOV was associated with a reduction in chronic lung disease, but in 2 trials, it was also associated with an increase in brain injury.1 These studies have been criticised for using different strategies to optimise lung expansion, possibly confounding the result.

The RCT by Johnson et al is 1 of 2 large, recent trials comparing HFOV with CV. While Johnson et al found no differences, Courtney et al found that infants ventilated with HFOV had a small but significant increase in survival without bronchopulmonary dysplasia, and were successfully extubated 1 week earlier.2 Intracranial abnormalities were not increased in either trial. However, Courtney et al found that those treated with HFOV had lower rates of lung haemorrhage,2 whereas Johnson et al found the rates were similar.

Factors that might account for these different findings include severity of illness at baseline, type of ventilator, and management of ventilation. Courtney et al included sicker infants, used one type of HFOV ventilator, and used stricter ventilation protocols;1 Johnson et al used 3 different types of HFOV ventilators that may have varied in performance characteristics and clinical effects,3 and management of ventilation was more representative of actual clinical practice.

In light of these discrepant findings, what should clinicians do? In settings where HFOV can be administered according to strict protocol, HFOV may be preferable. However, from a nursing perspective, the rigorous protocol needed for the care of an infant on HFOV, and the additional risks for infants arising from the possibility of inadvertent overdistension of the lungs, impaired cardiac output, and increased central venous pressure that might lead to intracranial haemorrhage, do not warrant its universal use.

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