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Elective high frequency jet ventilation versus conventional ventilation for respiratory distress syndrome in preterm infants (Review)

Bhuta T, Henderson-Smart DJ

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Elective high frequency jet ventilation versus conventional ventilation for respiratory distress syndrome in preterm infants (Review)

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[Intervention Review]

Elective high frequency jet ventilation versus conventional ventilation for respiratory distress syndrome in preterm infants

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ABSTRACT

Background

Pulmonary disease continues to be the major cause of mortality and morbidity in very low birth weight infants. Chronic lung disease (CLD) following mechanical ventilation for respiratory distress syndrome (RDS) is still a problem despite increased use of antenatal steroids and surfactant replacement therapy. Immaturity, barotrauma, volutrauma and oxygen toxicity are thought to be important factors in the cause of CLD. There is some evidence from animal and adult human studies that adequate ventilation can be achieved at lower pressures when using high frequency jet ventilation (HFJV, about 200-400 breaths per minute) compared to conventional ventilation (CV, 30-80 breaths per minute).

Objectives

The objective of this review was to determine whether the elective (commencing soon after initiation of mechanical ventilation) use of high frequency jet ventilation, as compared to conventional ventilation in preterm infants with respiratory distress syndrome (RDS), would decrease the incidence of chronic lung disease without adverse effects.

Search methods

Randomized trials from MEDLINE were identified by means of MeSH and text words 'high frequency ventilation', 'high frequency jet ventilation', 'jet ventilation' from the years 1980 to October 2002. The EMBASE database (1982-2002), the Oxford Database of Perinatal Trials, the Neonatal Trials Register of the Neonatal Review Group of the Cochrane Collaboration and The Cochrane Library (Issue 3, 2002) were also accessed.

Selection criteria

All randomized controlled trials of elective high frequency jet ventilation versus conventional ventilation in preterm infants born at less than 35 weeks GA or with a birth weight less than 2000 gms with respiratory distress were included in the systematic review. Trials which used HFJV to 'rescue' preterm infants due to severe respiratory distress usually beyond 24 hours, and trials that used HFJV for a mandatory time period and then switched back to CV, were not included in this review.

Data collection and analysis

The standard methods of the Neonatal Cochrane Review Group were used, including independent trial assessment and data extraction. Data were analysed using relative risk (RR) and risk difference (RD). From 1/RD the number needed to treat (NNT) for benefits and number needed to harm (NNH) for adverse outcomes were calculated.

Main results

Overall analysis of the three trials showed that HFJV is associated with a reduction in CLD at 36 weeks postmenstrual age in survivors [RR 0.58 (0.34, 0.98), RD -0.138 (-0.268, -0.007), NNT 7 (4, 90)]. The use of home oxygen therapy was evaluated in only one study (Keszler 1997) and a lower rate was found in the HFJV group [RR 0.24 (0.07, 0.79), RD -0.176 (-0.306, -0.047), NNT 5 (3, 21)]. Overall there was a trend towards an increase in the risk of PVL in the HFJV group, which was not significant. Subgroup analyses shows a significant increase in risk of PVL in the trial by Wiswell 1996 [RR 5.0 (1.19, 21.04), RD 0.250 (0.069, 0.431), NNH 4.0 (2.3,14.5)] where a 'low volume strategy' was the standard protocol for HFJV. In the other trial by Keszler 1997, where the intention was to use a 'high volume strategy', there was no significant difference in the incidence of PVL, RR 0.42 (0.14, 1.30).

In the overall analysis, there were no significant differences in the incidence of neonatal mortality, IVH all grades or in grades 3 or 4 IVH. In the subgroup where 'low volume strategy' was used there was a non-significant trend toward an increase in risk of IVH all grades and grades 3 or 4 IVH.

Authors' conclusions

The overall analysis shows a benefit in pulmonary outcomes in the group electively ventilated with HFJV. Of concern is the significant increase in acute brain injury in one trial which used lower mean airway pressures when ventilating with HFJV. There are as yet no long term pulmonary or neurodevelopmental outcomes from any of the trials.

PLAIN LANGUAGE SUMMARY

Elective high frequency jet ventilation versus conventional ventilation for respiratory distress syndrome in preterm infants

High frequency jet ventilation may help reduce chronic lung disease in preterm babies but adverse effects are unclear. Lung disease is a major cause of death in very low birth weight babies. Chronic lung disease (CLD) following mechanical ventilation for babies with breathing difficulties is also common. It is possible that the low gas exchange in newborns during breathing may help cause chronic lung disease. Elective high frequency jet ventilation (HFJV) is one type of mechanically assisted breathing method that may improve gas exchange in neonates without injuring the lung. The review of trials found there may be benefits of HFJV but not enough evidence of adverse effects. More research is needed.

BACKGROUND

Pulmonary disease continues to be the major cause of mortality and morbidity in very low birth weight infants. Chronic lung disease (CLD) following mechanical ventilation for respiratory distress syndrome (RDS) is still a problem despite increased use of antenatal steroids and surfactant replacement therapy. In addition to immaturity, barotrauma, volutrauma and oxygen toxicity during intermittent positive pressure ventilation are thought to be important factors in the cause of CLD (Ehrenkranz 1992, Jobe 2000).

There is evidence from animal studies (Barringer 1982, Carlon 1983, Hoff 1981) and adult studies (Carlon 1981 and Turnbull 1981) that high frequency jet ventilation (HFJV, 200 - 400 breaths per minute) may reduce the severity of lung injury during mechanical ventilation. Observational studies (Pokora 1983, Carlo 1984) suggested that HFJV may improve gas exchange in neonates with respiratory failure with lower pressures than conventional ventilation (CV).

OBJECTIVES

The objective of this review was to determine whether the elective use of high frequency jet ventilation (HFJV) as compared to conventional ventilation in preterm infants with RDS who were mechanically ventilated would decrease the incidence of chronic lung disease without adverse effects.

The following 'a priori' subgroup analyses were planned:

- 1) Trials with and without surfactant replacement therapy. Surfactant replacement therapy would be expected to increase alveolar recruitment, attenuate RDS and thus could alter treatment effects.
- 2) High and low volume ventilator strategies on HFJV. Ventilator strategies aimed at maintaining effective lung volume (high volume strategy, HVS) such as use of high mean airway pressures, manoeuvres to recruit alveolar volume after suctioning and weaning of FiO₂ before pressure would be expected to have better responses to treatment than those using a low volume strategy (LVS).
- 3) Infants at different gestational ages and birth weight, as they have different baseline rates of CLD and neurologic injury, may respond differently to the treatment.
- 4) Trials with and without adequate humidification. Different rates of necrotizing tracheitis and its consequences would be expected due to treatment.

METHODS

Criteria for considering studies for this review

Types of studies

All randomized controlled trials.

Types of participants

Preterm infants born at less than 35 weeks gestational age or with a birth weight of less than 2000 gms with pulmonary dysfunction, principally due to RDS and who were receiving IPPV.

Types of interventions

Included in the systematic review were trials in preterm infants which compared elective HFJV versus CV, with randomization early in the course of RDS soon after mechanical ventilation was commenced. Such trials were classified as 'Elective'. Trials were classified as 'Rescue', and excluded from this review, when patients were randomized after failure to adequately ventilate on CV or when complications of CV developed or were likely to develop. Trials that used HFJV for a mandatory short time period and then switched back to CV were not included in this review. The words 'conventional ventilation' (CV) implied time-cycled, pressure limited ventilation with respiratory rates of approximately 30-80/min.

Types of outcome measures

The following are the main outcomes sought in this review.

- 1) Mortality by 28-30 days, and before discharge.
- 2) Chronic lung disease defined as; a) supplemental oxygen or MV at 28d; or b) supplemental oxygen or MV at 36 weeks post-menstrual age (PMA)
- 3) Pulmonary air leak syndromes defined as presence of any of the following: pneumothorax, pulmonary interstitial emphysema or pneumoperitonium.
- 4) Intraventricular hemorrhages; a) all grades; b) grades 3 or 4
- 5) Periventricular leukomalacia
- 6) Periventricular echodensities
- 7) Necrotizing tracheobronchitis or subglottic stenosis
- 8) Pulmonary and neurodevelopmental outcomes in childhood

Search methods for identification of studies

Search was made of MEDLINE by means of the MeSH and text words, 'high frequency ventilation', 'high frequency jet ventilation', 'jet ventilation' from the years 1980 to October 2002; of EMBASE, and trials register held by the Neonatal Review Group of the Cochrane Collaboration (The Cochrane Library, Issue 3, 2002) and Oxford Database of Perinatal Trials. Information was also obtained from experts in the field and from cross references in published articles. Proceedings of Society for Pediatric Research/American Pediatric Society meetings were hand searched (1991-2002).

Data collection and analysis

The standard review methods of the Neonatal Review Group as documented in the Cochrane Library were used. This included independent quality assessment by the second author. Completeness of follow-up in this review is considered acceptable if less than 10% of subjects are excluded after randomization.

Additional data were obtained from Keszler 1997.

Methods used to collect data from the included trials:

Each author extracted data separately, then compared and resolved differences. Additional data were requested from authors as required.

Methods used to synthesize the data:

The standard method of the Neonatal Review Group was used, including for categorical data, use of relative risk (RR) and risk difference (RD). From 1/RD the number needed to treat (NNT) for benefits or number needed to harm (NNH) for adverse effects and

their 95% CI's were calculated. For continuous data, standardized mean difference with 95% CI was used.

RESULTS

Description of studies

Five randomized trials were identified. Three (Carlo 1990, Wiswell 1996 and Keszler 1997) were included in the systematic review. One trial (Carlo 1987) was not included since even though patients were randomized early, the intervention of HFJV was only for 48 hours after which they were switched back to conventional ventilation. Some of the results of this trial are discussed. One rescue trial (Keszler 1991) was also excluded.

In two trials the intention was to use a lower mean airway pressure (LVS) when switching from CV to HFJV (Carlo 1990, Wiswell 1996) while the third trial (Keszler 1997) the intention was to use a higher mean airway pressure (HVS).

Gestational age is normally calculated as postmenstrual age (PMA) at birth and together with postnatal age, is used here to define O2 dependency at 36 weeks. Wiswell 1996 and Keszler 1997 used the term postconceptual age but did not define it. This needs author clarification.

Surfactant was administered to infants in two trials (Wiswell 1996, Keszler 1997).

Details of each study are given in the Included Studies Table and in the references.

Risk of bias in included studies

Details of the methodological quality of each study are available in the Characteristics of Included Studies table. All trials concealed the randomization process and the treatment could not be blinded in any study. There were some post randomization losses to follow up in two trials (7% in Carlo 1990, 9% in Keszler 1997). Some infants were not assessed for the outcomes of IVH and PVL in the Keszler 1997 trial (6% in HFJV group and 9% in CV group). The primary outcomes of interest (CLD, IVH and PVL) were assessed blind in two studies (Wiswell 1996 and Keszler 1997) and this was unclear in the third (Carlo 1990).

Effects of interventions

Chronic Lung Disease (CLD)

In the overall analysis, there is a non-significant trend towards a reduction in the incidence of CLD at 28 days. There is a similar non-significant trend towards a reduction of CLD in the subgroup analyses where surfactant replacement therapy was used and also where a LVS was used.

CLD at 36 weeks PMA is significantly reduced in the two trials that assessed this outcome (Wiswell 1996 and Keszler 1997) both of which were also in the surfactant subgroup [summary RR 0.58 (0.34, 0.98); RD 0.138 (-0.268, -0.007), NNT 7 (4, 90)]. This outcome is also reduced in the trial (Keszler 1997) where high volume strategy was used [RR 0.50 (0.27, 0.92); RD -0.204 (-0.374, -0.034), NNT 7 (4, 90)]. The one trial (Wiswell 1996) that used a low volume strategy when on HFJV and reported CLD at 36 weeks PMA found no difference.

The use of home oxygen was assessed in only one study (Keszler 1997). The number of patients on home oxygen was found to be

lower in the HFJV group [RR 0.24 (0.07, 0.79); RD -0.176 (-0.306, -0.047), NNT 5 (3, 21)].

Air Leak Syndromes

There is no significant difference in incidence of air leak syndromes in the individual trials or in the overall analysis.

Neonatal Mortality

There is no significant difference in neonatal mortality in any individual trial, in the overall analysis, or in the subgroup analyses.

Intraventricular Hemorrhage (IVH)

There are no significant differences in the incidence of IVH of all grades in any individual trial or in the overall analysis. In the subgroup where low volume strategy was used there is a trend towards an increase in incidence of IVH. There are no significant differences in incidence of the more severe grades of IVH (3 or 4) in any individual trials or in the overall analyses [summary RR 1.37 (0.79, 2.37)]. In the subgroup where a low volume strategy was used only one trial reported IVH by grade (Wiswell 1996) and there is a non-significant trend towards an increase in grades 3 or 4 IVH. In the trial by Carlo 1990 progression to IVH grades 2 to 4 was reported as 9/21 in HFJV group and 7/21 in the CV group. However these figures include two patients in the HFJV group and seven patients in the CV group without initial head ultrasound who also developed grade 2 to 4 IVH. Thus these results were not included in the meta-analysis.

Periventricular Leukomalacia (PVL)

This outcome was reported in two studies (Wiswell 1996, Keszler 1997). Overall there is a non-significant trend towards an increase in risk [summary RR 1.24 (0.59, 2.61)] of PVL. In the one trial where a high volume strategy was intended (Keszler 1997) there is a trend towards a reduction in risk of PVL [RR 0.42 (0.14, 1.30)]. In the subgroup where a low volume strategy was used, only one trial (Wiswell 1996) reported PVL and there is a significant increase [RR 5.0 (1.19, 21.04), RD 0.250 (0.069, 0.0431), NNH 4.0 (2.3, 14.5)].

Periventricular Echodensities (PVE)

This outcome was assessed only in the Wiswell 1996 trial and no significant difference was found.

Continuous Data Outcomes

The following continuous outcomes were reported from the eligible trials and have been included after reviewing the studies. Keszler 1997 also reported medians and ranges for the continuous data since the data were not normally distributed.

Days in supplemental oxygen was assessed by all the trials as means and SD. The pooled results show a non-significant trend towards a decrease with HFJV. Keszler 1997 also reported the medians and ranges of days in supplemental oxygen [HFJV 37 (3-160) and CV 46 (3-167)].

Days on Mechanical ventilation (MV) is available from all three trials as means and SD. The pooled data gave a non-significant trend towards an increase in the days on MV. Keszler 1997 also reported the data as medians and ranges [HFJV 20 (3-96) and CV 26 (2-82)].

Wiswell 1996 reported a non-significant trend towards a decrease in length of hospital stay. Keszler 1997 reported the medians and ranges as 71 (24-198) for the HFJV group and 76 (33-167) for the CV group, which were not significantly different.

Two of the planned subgroup analyses could not be performed. There were no outcome data presented by gestational age or birth weight despite stratification at randomization in two of the studies (Wiswell 1996, Keszler 1997). Lack of humidification is now thought to be only of historical importance and was not a reported problem in any of the included trials.

DISCUSSION

It is possible that there are other trials which have not been published or have been published in a language not covered by this systematic review. This is a potential source of bias.

Pulmonary Outcomes

Overall this review suggests that the elective use of HFJV for preterm infants with RDS is associated with a reduction in measures of CLD such as oxygen or ventilator dependency at 36 weeks PMA and use of oxygen therapy at home. However, there are no long term pulmonary follow-up data from these studies. In the excluded trial (Carlo 1987) there were no differences in the incidence of CLD between the groups. During the 48 hour study period, 4/20 in the HFJV group and 8/20 in the CV developed one or more air leaks, this was, however, not significant.

Neurological Outcomes

Although there was no significant difference in short term brain injury in the overall analysis, subgroup analysis indicated that brain injury was more common when a 'low volume strategy' for HFJV was used (Wiswell 1996). The Keszler 1997 trial intended to use a 'high volume strategy' but this was actually used in only 56% of infants. Post hoc analyses indicated that the rate of acute brain injury such as grades 3 or 4 IVH was higher in the group who actually received a 'low volume strategy' (high volume strategy 3/34, 8.8% vs low volume strategy 6/27, 22.2%). There were no differences in the incidence of IVH developing during the 48 hour study period in the trial by Carlo 1987.

In the overall analysis there was a trend towards an increase in the incidence of PVL which was not significant. However, in the trial by Wiswell 1996 there was a significant increase in the incidence of PVL. In the report of this trial the logistic regression analysis of ventilator assignment showed that HFJV was independently associated with PVL. Hypocarbica was found not to be independently associated with any adverse outcomes in this trial although observational studies have suggested that marked hypocarbica is associated with an increased risk of cystic PVL (Calvert 1986, Graziani 1992, Fujimoto 1994).

The cause of acute neurological injury in some infants on HFJV is uncertain. This outcome has been reported from a single centre and the generalizability of this result is uncertain. The possible association with the use of a 'low volume strategy' during high frequency ventilation here has also been suggested in the review of trials evaluating high frequency oscillatory ventilation (Henderson-Smart 2002). The reason for this apparent association is unknown. To resolve the issue a randomized controlled trial comparing high and low volume strategies would be required. This is unlikely to be done given the current preference to use the 'high volume strategy', a strategy which has been recommended on the basis of animal studies (Froese 1991).

Benefits in terms of a reduction in CLD, where on an average seven infants would be needed to be treated to prevent CLD at 36 weeks in one infant, may be associated with increased risk of PVL, where for every four infants treated there would be one additional infant with PVL. This adverse effect is a 'worst case' scenario as it is based on one study (Wiswell 1996), and the other study (Keszler 1997) reporting this outcome showed a trend toward a reduction in PVL. Until these differences can be clarified it remains possible that the risks of elective HFJV may outweigh the benefits.

It is of concern that there were no long term neurodevelopmental outcomes available from any of these trials.

AUTHORS' CONCLUSIONS

Implications for practice

This review suggests that there may be benefits of elective HFJV in terms of reduction in risk of CLD at 28 days and 36 weeks PMA and at discharge. Of concern is the significant increase in adverse neurological outcomes in one of the trials which used lower mean airway pressures when ventilating with HFJV.

Implications for research

Future trials in populations at high risk of CLD, such as those born at less than 28 weeks or with a birthweight less than 1000 gms, are needed to clarify the safety and beneficial effects of elective HFJV. Long term pulmonary and neurological outcomes should be measured.

ACKNOWLEDGEMENTS

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10.1002/14651858.CD000328]

CHARACTERISTICS OF STUDIES

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

Carlo 1990

Methods	Single centre Concealment at randomization - Yes Blinding of intervention - No Complete followup - Yes (93%) Blinding of outcome - Can't tell
Participants	Forty-five preterm infants less than 24 hours of age with RDS and stratified into 3 groups; 1000-1250g, 1251-1500g, 1501-2000g
Interventions	HFJV, PIP and Paw decreased by 20% when changed to HFJV - low volume strategy (LVS), 250/min 1:3 IT:ET ratio; backup use of alternative intervention in both directions was permitted if failure documented on two consecutive ABG. Controls were ventilated with CV on time cycled pressure limited ventilators (Bear Cub). The protocol for CV was not specified.
Outcomes	Mortality at 28d, CLD at 28d, ALS, progression of IVH, success after crossover, days on MV, days on supplemental oxygen, MV at 28d.
Notes	Mean age at randomization 15.5 hrs for HFJV and 14 hrs for CV; enrollment stopped when there was no difference, no surfactant used.

Risk of bias

Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Keszler 1997

Methods	Multicentre trial; 8 centres Blinding of randomization -Yes Blinding of intervention - No Completeness of followup - Yes (91%); 14 patients from one centre were excluded from the analysis as they were simultaneously enrolled in another similar trial and reported in the study by Wiswell 1996 . Of 130 patients analysed, 61(94%) were assessed for IVH and PVL in the HFJV group and 59(91%) in CV group. Blinding of outcome measures -Yes
Participants	Reported on 130 of 144 preterm infants stratified into 3 groups 700-1500g, 1001-1250g, 1251-1500g; <36weeks gestational age; <20 hours of age and MV for <12 hours of age;
Interventions	HFJV Bunnell Life Pulse; concurrent CV used for humidification, positive end expiratory pressure (PEEP) for alveolar recruitment and to provide intermittent sigh breaths in form of background intermittent mandatory ventilation; at the time of randomization PEEP increased and this increased Paw 0.5 to 2 cms H2O, (HVS). CV was at rates between 30-60/min, inspiratory time of 0.3 to 0.4 sec and PEEP of 4 to 6 cms of water.

Keszler 1997 (Continued)

Outcomes	Mortality; CLD at 28d and 36 w PCA, O2 at discharge, days in O2, IVH all grades and grades 3 or 4, PVL, Days in hospital, crossover success	
Notes	Surfactant replacement therapy used. Although high volume strategy was the intended method, some centres used a low volume strategy (44% of infants). Concerns about adverse effects in some patients in another trial forced early stoppage of the trial. Mean age at randomisation 8.3+4.2 hrs, antenatal corticosteroids usage 30% CV vs 21% HFJV	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Wiswell 1996

Methods	Single centre Concealment of randomization -Yes Blinding of intervention - No Completeness of followup -Yes (100%) Blinding of outcome assessment -Yes	
Participants	Seventy-three infants less than 33 weeks GA, > 500 gms, < 2000 gms; < 24 hours of age; with RDS	
Interventions	HFJV (Bunnell Life Pulse) 420/min; PIP decreased to 80-90% of CV (LVS) when switched over, PEEP unchanged. Protocol for CV was not specified.	
Outcomes	IVH grades 3 or 4; IVH all grades; periventricular echodensities (PVE); cystic periventricular leukomalacia (CPVL); supplemental oxygen at 28d and 36 wk; mortality at 28d and 36wk; days on MV and days in hospital.	
Notes	Surfactant therapy used; backup use of the alternative intervention was allowed in both directions. Mean age at randomization 7.2+6 hrs., antenatal corticosteroids HFJV 22% CV 19%.	
<i>Risk of bias</i>		
Bias	Authors' judgement	Support for judgement
Allocation concealment?	Low risk	A - Adequate

Paw = Mean airway pressure, PEEP = positive end expiratory pressure, PIP = peak inspiratory pressure, HVS = high volume strategy, ALS = air leak syndrome

Characteristics of excluded studies [ordered by study ID]

Study	Reason for exclusion
Carlo 1987	Intervention commenced early but was only for 48 hours and then all the patients were switched back to conventional ventilation. The trial is therefore not comparable to trials where the intervention was intended to be used until extubation or failure to ventilate adequately. Infants with birth weights < 1000 gms, who are of most interest in this review because of their high rate of CLD, IVH and PVL, were excluded from the study.

Study	Reason for exclusion
Keszler 1991	Patients who developed pulmonary interstitial emphysema on conventional ventilation were randomized. This trial thus fulfilled the definition of rescue therapy and is the subject of another review.

DATA AND ANALYSES

Comparison 1. Elective HFJV vs CV

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 CLD at 28 d in survivors	3	204	Risk Ratio (M-H, Fixed, 95% CI)	0.90 [0.74, 1.09]
2 CLD at 36 w in survivors	2	170	Risk Ratio (M-H, Fixed, 95% CI)	0.59 [0.35, 0.99]
3 Air leak syndromes	2	172	Risk Ratio (M-H, Fixed, 95% CI)	0.82 [0.55, 1.22]
4 Home oxygen in survivors	1	107	Risk Ratio (M-H, Fixed, 95% CI)	0.24 [0.07, 0.79]
5 Neonatal mortality	3	245	Risk Ratio (M-H, Fixed, 95% CI)	0.86 [0.49, 1.50]
6 IVH all grades	2	193	Risk Ratio (M-H, Fixed, 95% CI)	1.07 [0.86, 1.35]
7 IVH grades 3 or 4	2	193	Risk Ratio (M-H, Fixed, 95% CI)	1.37 [0.79, 2.37]
8 Periventricular echodensities	1	73	Risk Ratio (M-H, Fixed, 95% CI)	1.10 [0.65, 1.86]
9 Periventricular leukomalacia	2	183	Risk Ratio (M-H, Fixed, 95% CI)	1.24 [0.59, 2.61]
10 Days in oxygen	3	245	Mean Difference (IV, Fixed, 95% CI)	-6.86 [-15.94, 2.22]
11 Days in hospital	2	203	Mean Difference (IV, Fixed, 95% CI)	-5.45 [-13.54, 2.64]
12 Days on IPPV	3	245	Mean Difference (IV, Fixed, 95% CI)	1.23 [-4.88, 7.33]

Analysis 1.1. Comparison 1 Elective HFJV vs CV, Outcome 1 CLD at 28 d in survivors.

Analysis 1.2. Comparison 1 Elective HFJV vs CV, Outcome 2 CLD at 36 w in survivors.

Analysis 1.3. Comparison 1 Elective HFJV vs CV, Outcome 3 Air leak syndromes.

Analysis 1.4. Comparison 1 Elective HFJV vs CV, Outcome 4 Home oxygen in survivors.

Analysis 1.5. Comparison 1 Elective HFJV vs CV, Outcome 5 Neonatal mortality.

Analysis 1.6. Comparison 1 Elective HFJV vs CV, Outcome 6 IVH all grades.

Analysis 1.7. Comparison 1 Elective HFJV vs CV, Outcome 7 IVH grades 3 or 4.

Analysis 1.8. Comparison 1 Elective HFJV vs CV, Outcome 8 Periventricular echodensities.

Analysis 1.9. Comparison 1 Elective HFJV vs CV, Outcome 9 Periventricular leukomalacia.

Analysis 1.10. Comparison 1 Elective HFJV vs CV, Outcome 10 Days in oxygen.

Analysis 1.11. Comparison 1 Elective HFJV vs CV, Outcome 11 Days in hospital.

Analysis 1.12. Comparison 1 Elective HFJV vs CV, Outcome 12 Days on IPPV.

Comparison 2. Elective HFJV vs CV with surfactant replacement therapy

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 CLD at 28 d in survivors	2	170	Risk Ratio (M-H, Fixed, 95% CI)	0.94 [0.77, 1.15]
2 CLD at 36 w in survivors	2	170	Risk Ratio (M-H, Fixed, 95% CI)	0.59 [0.35, 0.99]
3 Air leak syndromes	1	130	Risk Ratio (M-H, Fixed, 95% CI)	0.78 [0.47, 1.31]
4 Home oxygen in survivors	1	107	Risk Ratio (M-H, Fixed, 95% CI)	0.24 [0.07, 0.79]
5 Neonatal mortality	2	203	Risk Ratio (M-H, Fixed, 95% CI)	0.93 [0.50, 1.75]
6 IVH all grades	2	193	Risk Ratio (M-H, Fixed, 95% CI)	1.09 [0.84, 1.43]
7 IVH grades 3 or 4	2	193	Risk Ratio (M-H, Fixed, 95% CI)	1.37 [0.79, 2.37]
8 Periventricular echodensities	1	73	Risk Ratio (M-H, Fixed, 95% CI)	1.10 [0.65, 1.86]
9 Periventricular leukomalacia	2	183	Risk Ratio (M-H, Fixed, 95% CI)	1.24 [0.59, 2.61]
10 Days in oxygen	2	203	Mean Difference (IV, Fixed, 95% CI)	-6.85 [-16.20, 2.49]
11 Days in hospital	2	203	Mean Difference (IV, Fixed, 95% CI)	-5.45 [-13.54, 2.64]
12 Days on IPPV	2	203	Mean Difference (IV, Fixed, 95% CI)	0.32 [-6.47, 7.12]

Analysis 2.1. Comparison 2 Elective HFJV vs CV with surfactant replacement therapy, Outcome 1 CLD at 28 d in survivors.

Analysis 2.2. Comparison 2 Elective HFJV vs CV with surfactant replacement therapy, Outcome 2 CLD at 36 w in survivors.

Analysis 2.3. Comparison 2 Elective HFJV vs CV with surfactant replacement therapy, Outcome 3 Air leak syndromes.

Analysis 2.4. Comparison 2 Elective HFJV vs CV with surfactant replacement therapy, Outcome 4 Home oxygen in survivors.

Analysis 2.5. Comparison 2 Elective HFJV vs CV with surfactant replacement therapy, Outcome 5 Neonatal mortality.

Analysis 2.6. Comparison 2 Elective HFJV vs CV with surfactant replacement therapy, Outcome 6 IVH all grades.

Analysis 2.7. Comparison 2 Elective HFJV vs CV with surfactant replacement therapy, Outcome 7 IVH grades 3 or 4.

Analysis 2.8. Comparison 2 Elective HFJV vs CV with surfactant replacement therapy, Outcome 8 Periventricular echodensities.

Analysis 2.9. Comparison 2 Elective HFJV vs CV with surfactant replacement therapy, Outcome 9 Periventricular leukomalacia.

Analysis 2.10. Comparison 2 Elective HFJV vs CV with surfactant replacement therapy, Outcome 10 Days in oxygen.

Analysis 2.11. Comparison 2 Elective HFJV vs CV with surfactant replacement therapy, Outcome 11 Days in hospital.

Analysis 2.12. Comparison 2 Elective HFJV vs CV with surfactant replacement therapy, Outcome 12 Days on IPPV.

Comparison 3. Elective HFJV with low volume strategy

Outcome or subgroup title	No. of studies	No. of participants	Statistical method	Effect size
1 CLD at 28 d in survivors	2	97	Risk Ratio (M-H, Fixed, 95% CI)	0.84 [0.63, 1.13]
2 CLD at 36 w in survivors	1	63	Risk Ratio (M-H, Fixed, 95% CI)	0.88 [0.33, 2.34]
3 Air leak syndromes	1	42	Risk Ratio (M-H, Fixed, 95% CI)	0.91 [0.50, 1.67]
4 Home oxygen in survivors	0	0	Risk Ratio (M-H, Fixed, 95% CI)	0.0 [0.0, 0.0]
5 Neonatal mortality	2	115	Risk Ratio (M-H, Fixed, 95% CI)	0.98 [0.42, 2.31]
6 IVH all grades	1	73	Risk Ratio (M-H, Fixed, 95% CI)	1.25 [0.89, 1.76]
7 IVH grades 3 or 4	1	73	Risk Ratio (M-H, Fixed, 95% CI)	1.82 [0.88, 3.77]
8 Periventricular echodensities	1	73	Risk Ratio (M-H, Fixed, 95% CI)	1.10 [0.65, 1.86]
9 Periventricular leukomalacia	1	64	Risk Ratio (M-H, Fixed, 95% CI)	5.0 [1.19, 21.04]
10 Days in oxygen	2	115	Mean Difference (IV, Fixed, 95% CI)	-5.53 [-19.66, 8.60]
11 Days in hospital	1	73	Mean Difference (IV, Fixed, 95% CI)	32.90 [19.78, 46.02]
12 Days on IPPV	2	115	Mean Difference (IV, Fixed, 95% CI)	2.53 [-6.66, 11.71]

Analysis 3.1. Comparison 3 Elective HFJV with low volume strategy, Outcome 1 CLD at 28 d in survivors.

Analysis 3.2. Comparison 3 Elective HFJV with low volume strategy, Outcome 2 CLD at 36 w in survivors.

Analysis 3.3. Comparison 3 Elective HFJV with low volume strategy, Outcome 3 Air leak syndromes.

Analysis 3.5. Comparison 3 Elective HFJV with low volume strategy, Outcome 5 Neonatal mortality.

Analysis 3.6. Comparison 3 Elective HFJV with low volume strategy, Outcome 6 IVH all grades.

Analysis 3.7. Comparison 3 Elective HFJV with low volume strategy, Outcome 7 IVH grades 3 or 4.

Analysis 3.8. Comparison 3 Elective HFJV with low volume strategy, Outcome 8 Periventricular echodensities.

Analysis 3.9. Comparison 3 Elective HFJV with low volume strategy, Outcome 9 Periventricular leukomalacia.

Analysis 3.10. Comparison 3 Elective HFJV with low volume strategy, Outcome 10 Days in oxygen.

Analysis 3.11. Comparison 3 Elective HFJV with low volume strategy, Outcome 11 Days in hospital.

Analysis 3.12. Comparison 3 Elective HFJV with low volume strategy, Outcome 12 Days on IPPV.

WHAT'S NEW

Date	Event	Description
16 October 2008	Amended	Converted to new review format.

HISTORY

Protocol first published: Issue 2, 1998

Review first published: Issue 2, 1998

Date	Event	Description
16 January 1998	New citation required and conclusions have changed	Substantive amendment

CONTRIBUTIONS OF AUTHORS

Both authors participated in the development of the protocol. Tushar Bhuta carried out the literature searches. Both authors reviewed the trials and extracted the data. Tushar Bhuta entered the data into RevMan and wrote the review with editorial input from David Henderson-Smart.

DECLARATIONS OF INTEREST

None

SOURCES OF SUPPORT

Internal sources

- NSW Centre for Perinatal Health Services Research, University of Sydney, Australia.
- Department of Neonatology, Royal North Shore Hospital, Sydney, Australia.
- Royal Prince Alfred Hospital, Sydney, Australia.

External sources

- No sources of support supplied

INDEX TERMS

Medical Subject Headings (MeSH)

*High-Frequency Ventilation; Infant, Premature; Respiration, Artificial; Respiratory Distress Syndrome, Newborn [*therapy]

MeSH check words

Humans; Infant, Newborn