

Background

Preterm infants are at risk of respiratory distress syndrome (RDS) due to surfactant deficiency and this is associated with the need for respiratory support.⁴ Invasive mechanical ventilation (IMV) is associated with adverse effects, like bronchopulmonary dysplasia (BPD).² Non-invasive ventilation (NIV) is used to avoid IMV and associated complications.² NIV modes commonly used in preterm infants with RDS include nasal continuous positive airway pressure (NCPAP), biphasic NCPAP (BP-NCPAP), and nasal intermittent positive pressure ventilation (NIPPV).

High frequency oscillatory ventilation (HFOV) is a common IMV mode in neonatal care. Clinical knowledge and experience with HFOV and the trend towards NIV has resulted in non-invasive high frequency oscillatory ventilation (NIHFOV).³ NIHFOV is gaining popularity, but not yet routinely used.⁴ This review investigates current evidence comparing NIHFOV to other NIV modes in preterm infants with RDS.

Research Question

Population: Preterm infants with RDS

Intervention: NIHFOV

Comparison: Other modes of NIV

Outcome: Decrease the need for IMV, reduce the duration of NIV, and improve PCO₂ levels

“In preterm infants with RDS, does NIHFOV compared to other modes of NIV decrease the need for IMV, reduce the duration of NIV, and improve PCO₂ levels?”

Secondary Outcomes: BPD and mortality

Methods

Databases: PubMed, CINAHL, Embase, and Cochrane Library

Key terms: “preterm infants”, “respiratory distress syndrome”, and “non-invasive high frequency oscillatory ventilation” or “nasal high frequency oscillatory ventilation”

Filters Applied:

Publication Date: 10 years (2009-2019)

Species: Humans

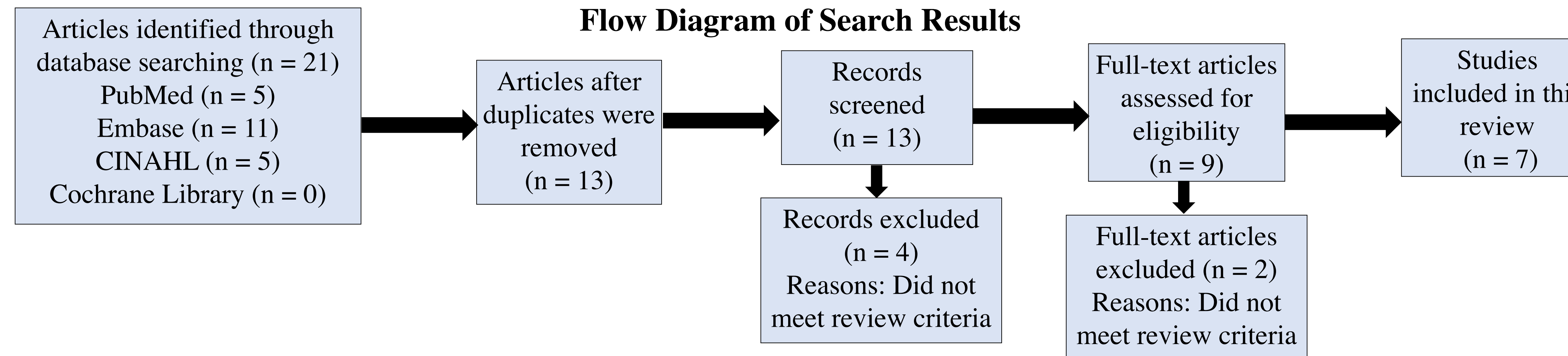
Language: English

Article Types: Randomized controlled trials (RCTs), systematic reviews (SRs), meta-analyses (MAs), clinical trials, and practice guidelines

Critical Appraisal: Supported through CONSORT, the Cochrane Handbook, PRISMA, and GRADE.

Results

Flow Diagram of Search Results



Article Summary Table

Study	Methods	Results	Limitations
Li et al. (2019) ⁶	SR + MA 8 trials, n=359 NIHFOV vs. NCPAP or BP-NCPAP	PCO ₂ levels (p<0.001), change in PCO ₂ levels (p<0.001), and rate of intubation (p<0.001) were significantly improved with NIHFOV	<ul style="list-style-type: none"> Limited number of trials with small sample sizes RCTs had differing study designs, interventions, and clinical characteristics of patients Majority of patients were > 30w gestation, but RDS remains prevalent in younger infants
Mukerji et al. (2017) ⁸	RCT n=39 16 NIHFOV & 23 BP-NCPAP	NIV failure was lower with NIHFOV, but not statistically significant (p=0.09). Intubation rate, BPD, mortality, duration of NIV, and CO ₂ gradient were statistically similar (p>0.05).	<ul style="list-style-type: none"> Small, pilot trial Different numbers of participants in the groups Limited to infants > 72hrs old who failed NCPAP, but this likely excluded many infants who failed prior
Zhu et al. (2017) ¹⁰	RCT n=76 37 NIHFOV & 39 NCPAP	Need for IMV was significantly reduced with NIHFOV (p=0.004). BPD (p=0.386) and mortality (p=0.525) were not statistically different.	<ul style="list-style-type: none"> Single-centre trial with small sample size Done in China, where there could be variations in practice Included infants 28-34w gestation, but RDS and benefits of NIV are still prevalent in younger infants
Malakian et al. (2019) ⁷	RCT n=128 64 NIHFOV & 64 NCPAP	Duration of respiratory support (p=0.009) and CO ₂ clearance (p=0.001) were statistically improved with NIHFOV. IMV (p=0.133) and mortality (p=0.518) were not statistically significant. BPD was not seen.	<ul style="list-style-type: none"> Single-centre trial with small sample size Done in Iran, where there could be variations in practice Unclear if there was allocation concealment Included infants 28-34w gestation and 1000-2000g, but RDS remains prevalent in younger/smaller infants
Iranpour et al. (2019) ⁵	RCT n=68 34 NIHFOV & 34 NCPAP	Duration of NIV (p=0.02) and need for intubation (p=0.03) were significantly reduced with NIHFOV. BPD was similar (p=0.23) and there was no mortality.	<ul style="list-style-type: none"> Small sample size Done in Iran where there could be variations in practice Participants excluded due to not enough ventilators Included infants 30-36^w gestation, but RDS and benefits of NIV are still prevalent in younger infants
Chen et al. (2019) ¹	RCT n=206 103 NIHFOV & 103 NCPAP	Re-intubation was significantly reduced with NIHFOV (p=0.002), but further analyses showed this was only in infants ≤32 weeks (p=0.004) and with ARDS (p=0.032). PaCO ₂ levels were reduced in all infants (p<0.001). BPD (p=0.498) and death (p=0.540) were statistically similar.	<ul style="list-style-type: none"> Single-centre in China where there could be variations in clinical practice Most participants were >28w gestation, but RDS and benefits of NIV are still prevalent in younger infants
Shehadeh (2019) ⁹	SR + MA 5 trials, n=270 NIHFOV vs. NCPAP	PCO ₂ clearance (p=0.002), IMV (p=0.003), and duration of NIV (p=0.009) were significantly improved with NIHFOV. Mortality (p=0.56) and BPD (p=0.38) were not significantly different.	<ul style="list-style-type: none"> Limited number of trials with small sample sizes Evidence was overall moderate quality with some aspects of the trials having a high risk of bias RCTs had varying outcomes and infant weights/gestation

Discussion

Overall, the research indicates that NIHFOV is effective in preterm infants with RDS for reducing IMV, the duration of NIV, and CO₂ retention compared to NCPAP. Mortality and BPD were similar, which is disappointing. However, these outcomes were not largely seen and the lower limit of gestational ages may have impacted this.

Various limitations/differences between the studies limited quality of evidence. There were small sample sizes, some aspects had a high risk of bias (e.g. blinding was not feasible due to the differences between the NIV modes), most participants were > 30w gestation, only one trial was done in Canada, and there were differences regarding the ventilator used and parameters for NIHFOV and NCPAP.

Future research is needed to address the gaps. Larger, multi-centre RCTs are needed. Research should involve infants with younger gestational ages and assess appropriate NIHFOV settings. Trials on NIHFOV vs. NIPPV are needed as well. There are 2 multi-centre trials underway on NIHFOV vs NCPAP vs NIPPV with large sample sizes (NCT03181958; NCT03842462).

Conclusion

NIHFOV is more effective than NCPAP for decreasing the need for IMV, reducing the duration of NIV, and improving CO₂ clearance in preterm infants with RDS. Mortality and BPD are comparable. However, due to limited quality and quantity of evidence, a concrete conclusion cannot be made. Nonetheless, it is recommended that health care professionals view NIHFOV as a primary mode of NIV. Further large, multi-centre, adequately powered trials are necessary to inform evidence-based care and develop guidelines.

References

- Chen, L., Wang, L., Ma, J., Feng, Z., Li, J., & Shi Y. (2019). Nasal high-frequency oscillatory ventilation in preterm infants with respiratory distress syndrome and ARDS after extubation: A randomized controlled trial. *Chest*, 155(4), 740-748. doi:10.1016/j.chest.2019.01.014
- Davidson, L. M., & Berkelhamer, S. K. (2017). Bronchopulmonary dysplasia: Chronic lung disease of infancy and long-term pulmonary outcomes. *Journal of Clinical Medicine*, 6(1), 4. doi:10.3390/jcm6010004
- De Luca, D., & Dell'Orto, V. (2016). Non-invasive high-frequency oscillatory ventilation in neonates: Review of physiology, biology and clinical data. *Archives of Disease in Childhood – Fetal and Neonatal Edition*, 101(6), F5650-F570. doi:10.1136/archdischild-2016-310664
- Holme, N., & Chetcuti, P. (2012). The pathophysiology of respiratory distress syndrome in neonates. *Pediatrics and Child Health*, 22(12), 507-512. doi:10.1016/j.paed.2012.09.001
- Iranpour, R., Armanian, A. -M., Abedi, A. -R., & Farajzadegan, Z. (2019). Nasal high-frequency oscillatory ventilation (nHFOV) versus nasal continuous positive airway pressure (NCPAP) as an initial therapy for respiratory distress syndrome (RDS) in preterm and near-term infants. *BMJ Paediatrics Open*, 3(1). doi:10.1136/bmjpo-2019-000443
- Li, J., Li, X., Huang, X., & Zhang, Z. (2019). Non-invasive high-frequency oscillatory ventilation as respiratory support in preterm infants: A meta-analysis of randomized controlled trials. *Respiratory Research*, 20(1), 58. doi: 10.1186/s12931-019-1023-0
- Malakian, A., Bashirzadkhabaz, S., Aramesh, M. -R., & Dehdashtian, M. (2018). Noninvasive high-frequency oscillatory ventilation versus nasal continuous positive airway pressure in preterm infants with respiratory distress syndrome: A randomized controlled trial. *The Journal of Maternal-Fetal & Neonatal Medicine*. Advance online publication. doi:10.1080/14767058.2018.1555810
- Mukerji, A., Sarmiento, K., Lee, B., Hassall, K., & Shah, V. (2017). Non-invasive high-frequency ventilation versus bi-phasic continuous positive airway pressure (BP-CPAP) following CPAP failure in infants < 1250g: A pilot randomized controlled trial. *Journal of Perinatology*, 37(1), 49-53. doi:10.1038/jp.2016.172
- Shehadeh, A. M. H. (2019). Non-invasive high flow oscillatory ventilation in comparison with nasal continuous positive pressure ventilation for respiratory distress syndrome, a literature review. *Journal of Maternal-Fetal & Neonatal Medicine*. Advance online publication. doi:10.1080/14767058.2019.1671332
- Zhu, X. -W., Zhao, J. -N., Tang, S. -F., Yan, J., & Shi Y. (2017). Noninvasive high-frequency oscillatory ventilation versus nasal continuous positive airway pressure in preterm infants with moderate-severe respiratory distress syndrome: A preliminary report. *Pediatric Pulmonology*, 52(8), 1038-1042. doi:10.1002/ppul.23755