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Research Article

Utilization and Outcome of High-Frequency Oscillatory Ventilation in Neonates and Premature Infants; Systematic Review

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Abstract

Study Aim: The study aim to compare HFOV with alternative breathing techniques in terms of clinical outcomes, complications, and long-term impacts, and to evaluate the effectiveness of HFOV in enhancing oxygenation, ventilation duration, and neonatal survival rates.

Method: The PRISMA guideline was followed in the course of our investigation. We looked for publications published between 2012 and 2024 using the electronic databases PubMed, Cochrane, and Scopus. Our search targeted cohort studies and randomized controlled trials; studies that evaluate various neonatal breathing techniques; studies that use quantitative outcome measures; and studies involving newborns with respiratory distress syndromes. We exclude studies involving older infants, children, or adults, case reports, editorials, expert comments, narrative reviews, studies that do not employ HFOV as the major intervention, and studies that do not compare HFOV to another ventilation method.

Result and Discussion: In newborns with severe respiratory distress, HFOV is a successful but not selective breathing technique that offers benefits in lung preservation and oxygenation; nevertheless, its impact on survival and long-term results is still up for discussion. Early initiation, usage in certain patients, and combination with other supportive therapies (surfactant therapy) result in improved outcomes for HFOV. Long-term follow-up research and randomized controlled trials are advised to enhance HFOV procedures, reduce complications, and improve neonate outcomes in general.

Keywords: High-Frequency Oscillatory Ventilation; Neonates; Premature Infants; Respiratory Distress Syndrome

Abbreviations

HFOV: High-Frequency Oscillatory Ventilation; CMV: Conventional Mechanical Ventilation; SIMV: Synchronized Intermittent Mandatory Ventilation; RDS: Respiratory Distress Syndrome; I:E ratio: Inspiratory to Expiratory Ratio; MAS: Meconium Aspiration Syndrome; ARDS: Acute Respiratory Distress Syndrome; HMD: Hyaline Membrane Disease; VILI: Ventilator-Induced Lung Injury; CLD: Chronic Lung Disease; BPD: Bronchopulmonary Dysplasia; IVH: Intraventricular Hemorrhage; VLBW: Very Low Birth Weight; PSV: Pressure Support Ventilation; OI: Oxygenation Index; FiO2: Fraction of Inspired Oxygen; NOS: Newcastle-Ottawa Scale; RCTs: randomized controlled trials; NICU: Neonatal Intensive Care Unit

Introduction

Over 75% of neonates delivered before 27 weeks of pregnancy need artificial breathing in some kind in order to survive [1]. Although survival rates for infants born very low-birth-weight (VLBW) or extremely preterm (less than 28 weeks) have risen, ventilator-induced lung damage continues to be a major cause of chronic lung disease (CLD) [2]. Effective oxygenation and lung ventilation are therefore essential for avoiding CLD.

Oxygen toxicity, ventilator-induced lung damage, and immature lungs are the main risk factors for the development of CLD [2,3]. Northway., *et al*. coined the term “bronchopulmonary dysplasia” (BPD) in 1967 [4], and it is still used to refer to infants who require oxygen more than 28 days after birth [5]. Although there are other contributing elements to the pathophysiology of BPD, intrusive mechanical ventilation is the main risk factor. BPD is the most frequent cause of morbidity of preterm. Because of this, studies have concentrated on lung protection techniques to prevent the development of CLD [4,5].

High-frequency oscillatory ventilation (HFOV) describes methods that provide an active, biphasic displacement of air during both expiration and inhalation. At first, a piston pump or an electromagnetically powered loudspeaker membrane with a steady bias flow in the patient circuit were used to generate pressure oscillations. While piston pumps can only produce sine waves with an I:E ratio of 1:1, membranes may produce a variety of waveforms with asymmetric I:E ratios. Modern hybrid ventilators that use opposing in- and expiratory flows or positive and negative pressure sources to produce fullactive expiration have changed this oscillation concept [3].

Our study aim to assess the efficacy of HFOV in improving oxygenation, ventilation duration, and survival rates in neonates, and to compare HFOV with other ventilation strategies in terms of clinical outcomes, complications, and long-term effects.

Method

Our study was conducted according to The Preferred Reporting Items for Systematic reviews and Meta-Analyses (PRISMA) statement [6]. We searched electronic databases (PubMed, Cochrane, and Scopus) for articles published in the period from 2012 to 2024. We include; Randomized controlled trials (RCTs) and cohort studies; Studies that compare different ventilation strategies in neonates; Studies with quantitative outcome measures (e.g., oxygenation, mortality, mechanical ventilation duration); studies include neonates (preterm or term) diagnosed with respiratory distress syndromes (meconium aspiration syndrome (MAS), respiratory distress syndrome (RDS), acute respiratory distress syndrome (ARDS), and hyaline membrane disease (HMD)). We exclude, case reports, expert opinions, editorials, narrative reviews, studies on older infants, children, or adults, studies that do not use HFOV as the primary intervention, and studies that do not compare HFOV to another ventilation strategy.

Two authors independently evaluated and selected publications based on the aforementioned criteria; disagreements were resolved by consensus with a third author. Studies that were discovered in different databases after screening were de-duplicated. The articles that passed the initial screening were reviewed in their entirety. In situations when only partial information was provided, results were derived from the reference standard. Data from included studies was extracted in a predesigned Google form with access for all authors. Information regarding the study citation, duration, design, outcome, methodology, participant’s characteristics, interventions, and main findings were collected.

Newcastle-Ottawa Scale (NOS) Classification Criteria was used to assess the quality of 3 of the included studies [7-9] (Table 1), the criteria evaluates the quality of cohort and case-control studies**.** High-Quality Study (≥7 points)**;** Moderate-Quality Study (5–6 points); and Low-Quality Study (≤4 points)**.** Quality of randomized controlled trials [10-12] assessed using Risk of Bias (RoB 2) for RCTs (Table 2).

Study	Selection (0-4)	Comparability (0-2)	Outcome (0-3)	Total Score (0-9)	Quality Rating
Chen., *et al.*	4	2	3	9	High
Liu., *et al.*	3	1	2	6	Moderate
Yang., *et al.*	3	1	2	6	Moderate

Table 1: Quality assessment according to Newcastle-Ottawa Scale (NOS).

Study	Bias Due to Randomization	Bias Due to Deviations from Intended Intervention	Bias Due to Missing Outcome Data	Bias in Measurement of Outcomes	Bias in Selection of the Reported Results	Overall Bias Judgment
Salvo., *et al.*	Low	Some concerns	Low	Low	Low	Some concerns
Singh., *et al.*	Low	Low	Low	Low	Low	Low
Sun., *et al.*	Low	Low	Low	Low	Low	Low

Table 2: Quality assessment according to Risk of Bias (RoB 2) for RCTs.

Result

We include 6 articles in this systematic review (Figure 1). The studies evaluate the efficacy of HFOV in comparison to CMV and other ventilation strategies in neonates with respiratory distress syndromes (RDS), MAS, and ARDS. These are a significant differences in oxygenation, ventilation duration, mortality rates, and long-term outcomes in neonates with different ventilation interventions.

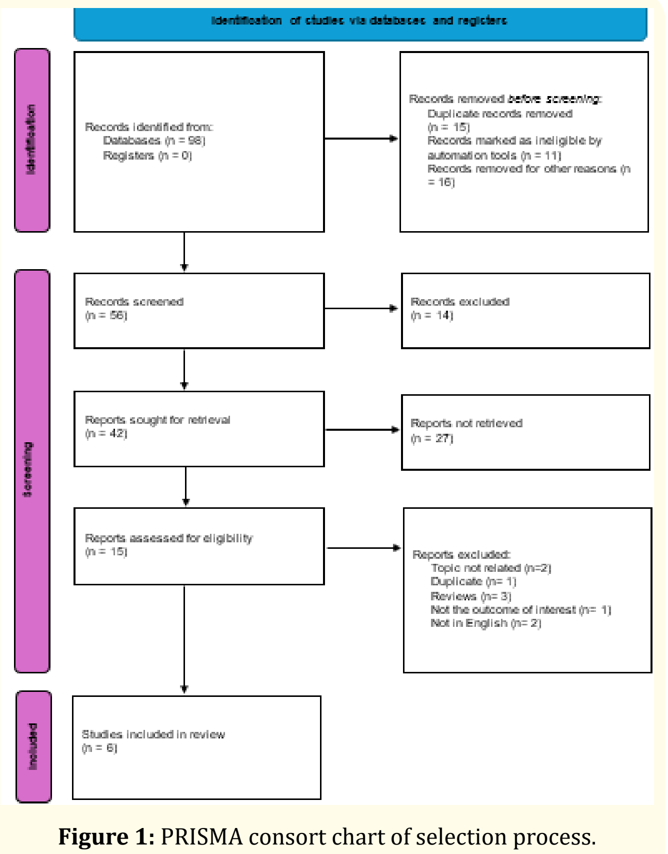

Figure 1: PRISMA consort chart of selection process.

Yang., *et al.* tested the use of HFOV vs CMV in neonates with severe MAS and ARDS. HFOV significantly improved lung ventilation, oxygenation, and decrease mechanical ventilation duration in relation to CMV. Air leakage incidence was lower in the HFOV group, it's a safer and effective treatment for neonates with severe respiratory distress. According to their findings the use of HFOV as an early intervention in severe MAS cases to prevent complications and improve survival rates.

Chen., *et al.* examined the combination of HFOV and pulmonary surfactant therapy in neonates with MAS. HFOV combined with surfactant improved oxygenation, reduced the need for prolonged mechanical ventilation, and decreased hospitalization duration in comparison to CMV alone. Early administration of surfactant in combination with HFOV provides better lung protection and enhances recovery in neonates with MAS. Liu., *et al.* retrospective propensity score-matched analysis compared HFOV and CMV in neonates with severe or moderate perinatal onset ARDS. HFOV was associated with a lower intraventricular hemorrhage (IVH) incidence, and it did not reduce mortality or bronchopulmonary dysplasia (BPD).

Salvo., *et al.* multicenter randomized controlled trial (RCT) conducted in very low birth weight (VLBW) infants diagnosed with RDS. HFOV reduced ventilator dependency, decreased the need for reintubation, and shortened hospital stays compared to CMV. Early initiation of HFOV in preterm infants improve short-term respiratory outcomes and reduce complications associated with prolonged mechanical ventilation. Singh., *et al.* compared HFOV with synchronized intermittent mandatory ventilation (SIMV) in preterm infants with HMD. HFOV show better early oxygenation and shorter hospital stays in comparison to SIMV. There was no significant difference in long-term complications or neurodevelopmental outcomes between the two groups. HFOV is a preferred initial ventilation strategy for neonates with HMD. Sun., *et al*. examined HFOV versus SIMV with pressure support ventilation (PSV) in preterm infants with severe RDS. HFOV reduced mortality, BPD rates, and improved long-term neurodevelopmental outcomes in comparison to SIMV with PSV. HFOV associated with shorter hospitalization duration.

Study	Study Aim	Sample Size	Targeted Population	Methodology
Chen., *et al*.	Evaluate the effects of HFOV combined with surfactant on MAS compared to CMV.	65 neonates	Neonates diagnosed with severe MAS requiring mechanical ventilation.	Retrospective cohort study comparing HFOV + surfactant vs. CMV.
Liu., *et al*.	Assess the impact of HFOV vs. CMV on neonatal ARDS outcomes using propensity score matching.	280 neonates	Neonates with severe or moderate perinatal onset ARDS requiring invasive ventilation.	Retrospective cohort study using one-to-one propensity score matching to compare HFOV vs. CMV.
Salvo., *et al*.	Compare the effectiveness of HFOV and CMV in premature infants with RDS.	450 premature infants	VLBW infants diagnosed with respiratory distress syndrome.	Multicenter randomized controlled trial comparing HFOV vs. CMV in premature infants with RDS.
Singh., *et al*.	Determine the efficacy of HFOV vs. SIMV in preterm neonates with HMD.	320 preterm neonates	Preterm neonates diagnosed with HMD requiring mechanical ventilation.	Randomized controlled trial comparing HFOV vs. SIMV in preterm neonates with HMD.
Sun., *et al*.	Investigate the clinical outcomes of HFOV vs. SIMV + PSV in preterm infants with severe RDS.	366 preterm infants	Preterm infants with severe RDS requiring mechanical ventilation.	Randomized controlled trial comparing HFOV vs. SIMV + PSV in preterm infants with severe RDS.
Yang., *et al*.	Evaluate the clinical effects of HFOV vs. CMV in neonates with MAS complicated by ARDS.	65 neonates	Neonates with severe MAS complicated by ARDS.	Retrospective cohort study comparing HFOV vs. CMV in neonates with MAS complicated by ARDS.

Table 3: Characteristics of the included studies.

Study	Study Design	Duration	Inclusion Criteria	Interventions Used	Main Findings	Outcome
Chen., *et al*.	Retrospective cohort study	2010 - 2013	Neonates with MAS requiring mechanical ventilation	Comparison of HFOV + surfactant vs. CMV	HFOV combined with surfactant improved oxygenation and reduced ventilation time compared to CMV.	HFOV+surfactant showed significant benefits for MAS, reducing ventilation time and hospital stay.
Liu., *et al*.	Retrospective analysis	2014 - 2018	Neonates with perinatal onset ARDS requiring invasive ventilation	Comparison of HFOV vs. CMV using propensity score matching	HFOV was associated with a lower incidence of IVH but did not significantly reduce mortality or BPD.	HFOV lowered IVH incidence but was not superior to CMV in reducing mortality or BPD.

Salvo., *et al*.	Randomized controlled trial	2004 - 2007	Very low birth weight (VLBW) infants with RDS without antenatal glucocorticoid prophylaxis	Comparison of HFOV vs. CMV in premature infants	HFOV reduced ventilator dependency, reintubation rates, and hospital stay compared to CMV in VLBW infants.	HFOV significantly reduced ventilator dependency and hospital stay in VLBW infants.
Singh., *et al*.	Randomized controlled trial	2007 - 2010	Preterm neonates with HMD requiring ventilation	Comparison of HFOV vs. SIMV in preterm neonates	HFOV show better early oxygenation and shorter hospital stays compared to SIMV in preterm neonates.	HFOV provided better oxygenation and shorter hospital stay than SIMV, with similar complication rates.
Sun., *et al*.	Randomized controlled trial	2007 - 2009	Preterm infants with severe RDS requiring mechanical ventilation within 24 hours of birth	Comparison of HFOV vs. SIMV + PSV in preterm infants with severe RDS	HFOV reduced death and BPD, improved long-term neurodevelopment, and decreased hospitalization duration.	HFOV reduced mortality, BPD, and improved neurodevelopmental outcomes in severe RDS preterm infants.
Yang., *et al*.	Retrospective cohort study	2018 - 2020	Neonates with severe MAS complicated with ARDS requiring mechanical ventilation	Comparison of HFOV vs. CMV in neonates with severe MAS and ARDS	HFOV improved lung ventilation, shortened mechanical ventilation time, and reduced air leakage incidence.	HFOV effectively improved oxygenation, reduced ventilation duration, and lowered air leakage incidence.

Table 4: *Main findings and outcomes of the included studies.*

Discussion

Our study provides a comprehensive review of HFOV as a ventilation strategy in neonates with RDS, MAS, and ARDS. The study discussed the main findings on efficacy, safety, clinical applicability, and long-term outcomes of HFOV in comparison to conventional mechanical ventilation (CMV).

HFOV maintain lung volume and reduce ventilator-induced lung injury (VILI) [3,13]. HFOV leads to better oxygenation and carbon dioxide clearance due to its ability to deliver small tidal volumes at supra-physiological frequencies. HFOV was associated with improved neuromotor outcomes in preterm infants at a corrected age of two years, with initial concerns about increased intra-ventricular hemorrhage (IVH) [14]. HFOV is better than conventional ventilation in decreasing mortality rates. There is a higher incidence of air leaks and pulmonary complications with HFOV, raising concerns about its widespread adoption [15]. HFOV is a rescue therapy for preterm neonates with severe refractory respiratory failure, it improves oxygenation indices (OI) and reduces FiO2 requirements within 24–48 hours, show its effectiveness in critically ill infants. The overall mortality rate still high at 34.7%, indicating that HFOV is a valuable intervention, but it's not completely mitigate the severity of respiratory failure in some cases [16]. HFOV can be used as a rescue therapy in patients who fail conventional mechanical ventilation. HFOV is associated with higher sedation and longer hospital stays, which could affect clinical decision-making [17].

Salvo., *et al*. (2012) and Cools., *et al*. (2015), advised to apply HFOV early as an alternative to conventional ventilation in neonates with severe RDS. HFOV improves oxygenation, reduces ventilator-induced lung injury (VILI), and lowers the risk of bronchopulmonary dysplasia (BPD) [10,13]. According to Liu., *et al*. study, HFOV was not better than CMV in decreasing mortality or the need for supplemental oxygen at discharge, indicating that patient selection criteria affect treatment outcomes [9]. HFOV improved lung function and shortened mechanical ventilation duration in neonates with MAS complicated by ARDS [7]. HFOV with surfactant administration additionally improve oxygenation and decrease hospitalization period in relation to CMV alone [8]. According to Wang., *et al*. (2015) meta-analysis HFOV's is better than CMV, with some of their included studies show a higher rates of air leaks, hemodynamic instability, and prolonged ventilation in certain cases that ventilator settings, patient selection, and HFOV protocols play a important role in determining the success.

HFOV had a potential risk of complications, such as; air leaks, overdistension, and hemodynamic compromise. According to Truffert., *et al*. (2007) study HFOV did not reduce chronic lung disease [14]. Sun., *et al*. study, found that HFOV decrease mortality and BPD but did not eliminate the risk of long-term pulmonary complications [12]. HFOV associate with higher sedation and prolonged hospital stays, which affect clinical decision-making [17], and according to Liu., *et al*. study, HFOV patients needed longer NICU stays in relation to CMV patients, especially in neonates with pre-existing lung pathology.

Study limitations

Our study had some limitations as the included articles directed toward neonates with MAS, ARDS, RDS, or HMD, and not represent all neonatal populations, such as those with mild or borderline respiratory distress. Variation in inclusion criteria in studies result in heterogeneity in patient severity, which affect comparisons. Limited long-term data, as most studies discussed short-term outcomes (oxygenation, ventilation duration, and survival rates) and lack follow-up on long term outcome (neurodevelopmental outcomes, lung function in childhood, and long-term quality of life).

Conclusion

HFOV is effective but selective ventilation method in neonates with severe respiratory distress, it demonstrates advantages in oxygenation and lung protection, its effect on survival and long-term outcomes still debated. HFOV produce better effect when early initiated, used in selected patients, and combined with other supportive interventions (surfactant therapy). Large-scale randomized controlled trials and long-term follow-up studies are recommended to improve HFOV protocols, decrease complications, and improve overall neonatal outcomes.

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