Published Online: 2026 April 29

Research Article

Effect of High-frequency Oscillatory Ventilation-Assisted Pulmonary Surfactant Intervention on Children with Neonatal Respiratory Distress Syndrome

Mingxi Chen [1], Hao Wang [1], Wenjuan Zhang [1, *]

[1] Inner Mongolia Autonomous Region People's Hospital, Hohhot, China

[*] ***Corresponding Author:*** Inner Mongolia Autonomous Region People's Hospital, Hohhot, China. Email: zhangwjimarph@ph-edu.cn

Received: 2 March, 2025; **Revised:** 28 December, 2025; **Accepted:** 15 March, 2026

Abstract

Background: Neonatal respiratory distress syndrome (NRDS), also known as neonatal lung hyaline membrane disease, predominantly occurs in premature infants and remains a major cause of neonatal morbidity and mortality.

Objectives: This study aimed to evaluate the therapeutic efficacy of high-frequency oscillatory ventilation (HFOV) combined with pulmonary surfactant (PS) therapy in neonates with NRDS.

Methods: A total of 100 neonates diagnosed with NRDS were retrospectively enrolled from patients admitted to our hospital between March 2022 and February 2024. Patients were divided into an observation group (n = 50; HFOV-assisted PS therapy) and a control group (n = 50; PS therapy alone). Baseline demographic and clinical characteristics were comparable between the 2 groups. Clinical outcomes, blood gas parameters, and complication rates were analyzed.

Results: Compared with the control group, the observation group had a significantly lower overall complication rate ($P < 0.05$). After treatment, the observation group demonstrated increased arterial partial pressure of oxygen (PaO_2) and reduced partial pressure of carbon dioxide (PCO_2) compared with the control group ($P < 0.05$). In addition, arterial oxygen saturation (SaO_2) was significantly decreased after HFOV-assisted PS therapy compared with the control group ($P < 0.05$). The durations of mechanical ventilation and total hospital stay were both significantly shorter in the observation group than in the control group ($P < 0.05$).

Conclusions: High-frequency oscillatory ventilation-assisted PS therapy was associated with improved blood gas parameters, shorter durations of mechanical ventilation and hospitalization, and a reduced risk of complications in neonates with NRDS. These findings suggest that HFOV combined with PS represents an effective therapeutic strategy for the clinical management of NRDS.Keywords:

1. Background

Neonatal respiratory distress syndrome (NRDS), also known as neonatal lung hyaline membrane disease, is mainly observed in premature infants. Pulmonary surfactant (PS) synthesis and secretion normally begin during the last trimester of fetal lung development. However, in premature infants, lung immaturity results in insufficient PS production, leading to increased alveolar surface tension, alveolar collapse, and impaired gas exchange (1, 2). With the continuous advancement of perinatal medical technologies, the survival rate of neonates has progressively increased. Nevertheless, the incidence of NRDS has not shown a corresponding decline and remains one of the leading causes of neonatal mortality and long-term complications (3). In the treatment of NRDS, PS replacement therapy and mechanical ventilation constitute the cornerstones of treatment. Pulmonary surfactant, secreted by type II alveolar epithelial cells, is primarily composed of phospholipids and proteins, among which dipalmitoyl phosphatidylcholine plays a critical role. This component forms a monomolecular layer at the alveolar air-liquid interface, effectively reducing surface tension (4, 5). Although conventional mechanical ventilation can improve overall oxygenation to a certain

How to Cite: Chen M, Wang H, Zhang W. Effect of High-frequency Oscillatory Ventilation-Assisted Pulmonary Surfactant Intervention on Children with Neonatal Respiratory Distress Syndrome. Inn J Pediatr. 2026;36(3):e160903. doi: https://doi.org/10.5812/ijpediatr-160903

extent, it is also associated with ventilator-induced lung injuries, such as barotrauma and volutrauma, which may adversely affect long-term pulmonary development in neonates. High-frequency oscillatory ventilation (HFOV), characterized by low tidal volume, low airway pressure, and high frequency, has been proposed as an alternative ventilation strategy with the potential to minimize lung injury caused by mechanical ventilation, thereby offering new therapeutic perspectives for the treatment of NRDS (6).

In recent years, the combined application of HFOV and PS therapy has gradually emerged as a research focus in the treatment of NRDS, driven by ongoing advances in neonatal intensive care. Existing studies suggest that this combined approach may provide significant benefits in improving oxygenation, shortening the duration of mechanical ventilation, and reducing complication rates (7). However, the optimal timing, dosage, and overall clinical efficacy of HFOV-assisted PS therapy remain controversial, and uniform clinical standards or consensus guidelines have not yet been established.

2. Objectives

The present study was designed to evaluate the effect of HFOV-assisted PS therapy in neonates with NRDS.

3. Methods

3.1. Subjects

This study was designed as a retrospective analysis of real-world clinical data because prospective randomization of ventilation strategies was not feasible in the emergency management of NRDS. Therefore, the sample size was determined by the number of eligible patients meeting the inclusion criteria during the study period. The final cohort of 100 neonates was comparable in size to those reported in previous single-center studies evaluating HFOV- or PS-based interventions in NRDS and was considered appropriate for exploratory comparative analyses.

A total of 100 neonates diagnosed with NRDS and admitted to our hospital between March 2022 and February 2024 were retrospectively enrolled in this study. Patients were assigned to the control or observation group according to the ventilation strategy actually applied during routine clinical management rather than by randomization. Specifically, neonates who received PS therapy alone were included in the control group (n = 50), whereas those who received HFOV-assisted PS therapy were included in the observation group (n = 50). In the control group, there were 31 boys and 19 girls, with a postnatal age of 6 - 9 hours (7.21 ± 1.20 hours) and a birth weight of 1 - 3 kg (1.95 ± 0.11 kg). According to chest X-ray grading, 27 cases were classified as grade I NRDS and 23 cases as grade II NRDS. The observation group included 30 boys and 20 girls, with a postnatal age of 6 - 9 hours (7.19 ± 1.19 hours) and a birth weight of 1 - 3 kg (1.93 ± 0.13 kg). Chest X-ray grading showed 26 cases of grade I NRDS and 24 cases of grade II NRDS. Baseline characteristics were comparable between the 2 groups, and no statistically significant differences were observed ($P > 0.05$), indicating suitability for comparative analysis. Although retrospective group assignment may introduce selection bias, this risk was partly mitigated by the application of uniform inclusion and exclusion criteria and the comparability of baseline characteristics between groups; nevertheless, residual confounding cannot be completely excluded.

This study was approved by the Ethics Committee of the hospital, and informed consent was obtained retrospectively from the parents or legal guardians of the neonates during hospitalization or follow-up in accordance with institutional ethical requirements. This study was conducted and reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for observational studies.

The inclusion criteria were as follows: (1) Diagnosis of NRDS confirmed by chest computed tomography (CT) and/or other imaging examinations; (2) birth weight ≥ 1600 g; (3) postnatal age < 48 hours; (4) grade I - II NRDS based on chest X-ray findings; and (5) written informed consent obtained from parents or legal guardians.

The exclusion criteria were as follows: (1) Severe hepatic or renal diseases, including renal failure; or (2) leukemia or other severe systemic immune diseases. Retrospective assignment to groups may introduce selection bias, which was mitigated by matched baseline characteristics.

3.2. Pulmonary Surfactant Intervention Method for the Control Group

Pulmonary surfactant therapy was administered as follows. Neonates were placed in a neonatal intensive care unit (NICU) incubator and continuously monitored using an electrocardiogram (ECG) monitor for heart rate, respiratory rate, and oxygen saturation. The type and dosage of PS were calculated according to body weight. Calf Pulmonary Surfactant for Injection (CR Double-Crane Pharmaceuticals Co., Ltd.; approval no. NMPN H20052128; specification, 70 mg) was used. Before administration, airway secretions were aspirated, and a drug delivery catheter, sterile syringe, and appropriate endotracheal intubation equipment were prepared. The reconstituted PS solution was drawn into a sterile syringe at an initial dose of 100 - 200 mg/kg, and the dosage was double-checked to ensure accuracy. The syringe was then connected to the endotracheal tube, and PS was slowly and evenly administered by bolus injection, with the entire dose delivered within 10 - 15 seconds. Afterwards, endotracheal intubation was performed under aseptic conditions using a tube appropriate for the infant's weight and age. Pulmonary surfactant was administered into the trachea in 2 - 4 aliquots, with the infant's head slightly elevated and alternately tilted. Manual positive-pressure ventilation using a resuscitation bag was immediately applied after each aliquot to facilitate uniform pulmonary distribution of the surfactant. Ventilation parameters were adjusted based on blood gas results, targeting PaO_2 of 60 - 80 mmHg and PCO_2 of 35 - 45 mmHg.

3.3. High-Frequency Oscillatory Ventilation-Assisted Pulmonary Surfactant Intervention Method for the Observation Group

In the observation group, HFOV-assisted PS therapy was applied. After vital sign monitoring, endotracheal intubation, and PS administration identical to those used in the control group, the endotracheal tube was promptly connected to a high-frequency oscillatory ventilator. Initial ventilator parameters were set according to body weight and clinical condition as follows: Oscillation frequency, 10 - 15 Hz; amplitude, 20 - 40 cmH_2O, adjusted to achieve visible chest vibration; mean airway pressure (MAP), initially 2 - 5 cmH_2O above conventional levels and generally maintained at 10 - 20 cmH_2O; inspiratory time, 0.3 - 0.5 seconds, representing 30% - 50% of the oscillatory cycle; and fraction of inspired oxygen (FiO_2), 0.6 - 1.0, adjusted based on oxygen saturation and blood gas results. Oxygen saturation and ventilator parameters were continuously monitored, and oscillation frequency and amplitude were adjusted as needed. Ventilator settings, including MAP, oscillation frequency, amplitude, and FiO_2, were recorded every 15 - 30 minutes, and dynamic parameter charts were generated. Arterial blood gas analysis was reassessed every 4 - 6 hours or more frequently if clinically indicated, and ventilator parameters were individually optimized according to the results. High-frequency oscillatory ventilation parameter adjustments were guided by predefined clinical criteria, primarily based on arterial blood gas targets and oxygenation status: MAP and FiO_2 were titrated to maintain PaO_2 within 60 - 80 mmHg and adequate oxygen saturation, whereas oscillation amplitude and frequency were adjusted to maintain PCO_2 within 35 - 45 mmHg and ensure effective chest vibration. Detailed parameter ranges and optimization principles are provided in the Supplementary File.

3.4. Observation Indicators and Assessment Criteria

Clinical treatment indicators, including duration of mechanical ventilation and total length of stay, were recorded and compared between groups.

Blood gas parameters were measured before and after treatment using a blood gas analyzer and included PaO_2 (normal range, 55 - 80 mmHg), PCO_2 (normal range, 35 - 45 mmHg), and SaO_2 (normal range, 95% - 98%). Complications, including barotrauma, pulmonary air leak, and infection, were recorded. Outcome assessments were conducted by attending physicians using predefined clinical criteria. Owing to the retrospective design and the nature of the ventilation strategies, outcome assessors were not blinded to treatment allocation. The complication rate was calculated as follows: (Number of cases with barotrauma + number of cases with pulmonary air leak + number of cases with infection) / total number of cases × 100%.

3.5. Statistical Analysis

Data were analyzed using Statistical Package for the Social Sciences (SPSS) version 26.0 software. Count data, including complication rates, were expressed as n (%) and analyzed using the χ^2 test. For continuous variables, normality was assessed using the Shapiro-Wilk test, and homogeneity of variance was evaluated using Levene's test. Continuous data that satisfied these assumptions were expressed as mean ± standard deviation ($\bar{x} \pm SD$). Independent-sample t-tests were used for intergroup comparisons, and paired t-tests were applied for intragroup comparisons before and after treatment. In addition to P-values, effect sizes were calculated using Cohen's d to quantify the magnitude of differences, and corresponding 95% confidence intervals (CIs) were reported. $P < 0.05$ indicated statistical significance.

4. Results

4.1. Clinical Treatment Indicators

In the between-group comparison after treatment, the observation group exhibited a significantly shorter duration of mechanical ventilation than the control group (mean difference, -1.30 days; 95% CI, -2.03 to -0.57; Cohen's d = 0.70; P = 0.001). Similarly, the total length of

Table 1. Clinical Treatment Indicators ($\bar{x} \pm SD$, d) [a]

Groups	Duration of Mechanical Ventilation	Length of Stay
Observation (n = 50)	12.45 ± 1.92	29.44 ± 2.94
Control (n = 50)	13.75 ± 1.78	31.61 ± 3.22
Mean difference [b]	-1.30 (-2.03 to -0.57)	-2.17 (-3.38 to -0.96)
Effect size [c]	0.70	0.70
t	3.511	3.519
P-value [d]	0.001	0.001

[a] Values are presented as mean ± standard deviation.

[b] Mean differences were calculated as the observation group minus the control group, with corresponding 95% CIs.

[c] Effect sizes are expressed as Cohen's d.

[d] P-values were derived from independent-sample *t*-tests.

hospital stay was significantly reduced in the observation group compared with the control group (mean difference, -2.17 days; 95% CI, -3.38 to -0.96; Cohen's d = 0.70; P = 0.001) (Table 1).

4.2. Levels of Blood Gas Indicators

No statistically significant differences were observed in blood gas parameters between the 2 groups before treatment (P > 0.05). In the between-group comparison after treatment, the observation group showed lower PCO_2 (mean difference, -2.06 mmHg; 95% CI, -3.74 to -0.38; Cohen's d = 0.48) and lower SaO_2 (mean difference, -3.29%; 95% CI, -5.12 to -1.46; Cohen's d = 0.71), whereas PaO_2 (mean difference, 3.22 mmHg; 95% CI, 1.33 to 5.11; Cohen's d = 0.67) was increased compared with the control group (all P < 0.05) (Table 2).

4.3. Complication Rate

In the between-group comparison after treatment, the overall complication rate was significantly lower in the observation group than in the control group (2.0% vs. 14.0%; relative risk, 0.14; 95% CI, 0.02 - 1.08; P = 0.027) (Table 3).

5. Discussion

Neonatal respiratory distress syndrome is a severe respiratory disorder and remains a major focus in neonatal medicine and clinical practice. Epidemiological studies have demonstrated a global increase in the proportion of premature births, and NRDS continues to be one of the leading causes of morbidity, mortality, and long-term complications in premature infants, severely affecting survival quality and prognosis (8, 9). The pathological basis of NRDS lies primarily in pulmonary immaturity, resulting in insufficient synthesis and secretion of PS. Severe PS deficiency may lead to hypoxemia and respiratory failure. Exogenous PS replacement therapy is therefore a cornerstone of NRDS management and has been shown to significantly improve respiratory function and reduce mortality. However, mechanical ventilation is still required in critically ill neonates (10).

Mechanical ventilation plays a central role in NRDS treatment, and HFOV represents a novel ventilation strategy. By maintaining airway pressure through high-frequency oscillation with extremely low tidal volumes, HFOV can reduce ventilator-induced lung injury, improve gas exchange, facilitate uniform PS distribution, lower alveolar surface tension, enhance alveolar compliance and stability, and ultimately improve therapeutic efficacy (11). Recent systematic reviews and meta-analyses have evaluated the role of HFOV in neonatal respiratory failure, with mixed results. A 2022 Cochrane meta-analysis comparing HFOV with conventional ventilation in preterm infants with respiratory distress syndrome (RDS) reported no consistent reduction in mortality but suggested a potential benefit in reducing air leak syndromes, particularly when lung-protective strategies were applied (12). Similarly, a 2023 meta-analysis focusing on early HFOV initiation indicated improved oxygenation indices without a clear survival advantage (13). These findings suggest that the benefits of HFOV are likely context-dependent rather than universally generalizable.

In the present study, 100 neonates with NRDS were retrospectively analyzed to evaluate the efficacy of HFOV-assisted PS therapy. The results demonstrated that SaO_2 and PCO_2 were significantly decreased, whereas PaO_2 was increased in the observation group compared with the control group (P < 0.05). These findings are

Table 2. Levels of Blood Gas Indicators ($\bar{x} \pm SD$) [a]

Groups	PCO_2 Before Treatment (mmHg)	PCO_2 After Treatment (mmHg)	SaO_2 Before Treatment (%)	SaO_2 After Treatment (%)	PaO_2 Before Treatment (mmHg)	PaO_2 After Treatment (mmHg)
Observation (n = 50)	28.63 ± 3.51	34.38 ± 4.07	73.11 ± 3.37	92.93 ± 4.91	49.21 ± 5.29	62.78 ± 4.89
Control (n = 50)	28.71 ± 3.45	36.44 ± 4.45	73.21 ± 3.41	96.22 ± 4.42	49.75 ± 5.32	59.56 ± 4.67
Mean difference [b]	—	-2.06 (-3.74 to -0.38)	—	-3.29 (-5.12 to -1.46)	—	3.22 (1.33 to 5.11)
Effect size [c]	—	0.48	—	0.71	—	0.67
Percent change [d]	—	5.7 decrease	—	3.4 decrease	—	5.4 increase
t	0.115	2.415	0.147	3.521	0.509	3.367
P-value [e]	0.909	0.018	0.883	0.001	0.612	0.001

Abbreviations: PCO_2, partial pressure of carbon dioxide; SaO_2, arterial oxygen saturation; PaO_2, arterial partial pressure of oxygen.

[a] Values are presented as mean ± standard deviation.

[b] Mean differences were calculated based on posttreatment values as the observation group minus the control group, with corresponding 95% CIs.

[c] Effect sizes are expressed as Cohen's d.

[d] Percent change represents the relative difference in posttreatment values between groups, calculated as (control - observation)/control × 100%.

[e] P-values were derived from independent-sample *t*-tests.

consistent with recent randomized controlled trials reporting improved gas exchange parameters when HFOV is combined with early or repeated PS administration compared with PS therapy alone (14, 15). Mechanistically, exogenous PS rapidly reduces alveolar surface tension, stabilizes alveolar structure, prevents end-expiratory alveolar collapse, and increases functional residual capacity. High-frequency oscillatory ventilation, in turn, maintains alveolar recruitment under relatively low tidal volumes and stable MAP, creating optimal conditions for sustained alveolar patency and homogeneous PS distribution. However, these mechanistic advantages should be interpreted within the context of the specific patient population and treatment timing examined in this study.

Additionally, an appropriately elevated effective MAP increases the proportion of alveoli recruited for gas exchange, thereby expanding the effective oxygen diffusion surface and contributing to higher PaO_2 levels. Through these complementary mechanisms, HFOV-assisted PS therapy facilitates correction of hypoxemia and supports the maintenance of SaO_2 within a physiological range (16, 17). Compared with conventional ventilation, HFOV enables efficient gas exchange at substantially lower tidal volumes, reduces dead-space ventilation, and enhances carbon dioxide elimination, thereby maintaining $PaCO_2$ within normal limits. Pulmonary surfactant supplementation further optimizes alveolar mechanics and gas exchange efficiency, which may synergistically promote CO_2 excretion (18). Although these mechanisms provide a plausible explanation for the observed physiological improvements, they do not necessarily imply equivalent clinical benefits across all NRDS populations or care settings.

Consistent with these mechanisms, the present study demonstrated significantly shorter durations of mechanical ventilation and hospital stay in the observation group. However, not all studies have reported unequivocal benefits of HFOV combined with PS. Several studies have shown neutral effects on major clinical outcomes, such as mortality or bronchopulmonary dysplasia, particularly when HFOV was applied late or in less severe cases of NRDS (19, 20). These discrepancies highlight the importance of patient selection, early intervention, and ventilation parameter optimization and caution against extrapolating our findings beyond similar clinical contexts.

Importantly, the complication rate was significantly lower in the observation group ($P < 0.05$). This observation aligns with recent evidence indicating that lung-protective ventilation strategies, including HFOV, may reduce the incidence of barotrauma and air leak syndromes compared with conventional ventilation (21, 22). High-frequency oscillatory ventilation minimizes alveolar overdistension and pressure fluctuations, while PS supplementation enhances alveolar stability, together reducing susceptibility to air leak and pressure-related lung injury (23-25). Emerging studies also suggest that PS participates in pulmonary immune defense, regulating immune cell activity, enhancing phagocytosis, and inhibiting pathogen adhesion and

Table 3. Complication Rate (%) [a, b]

Groups	Barotrauma (N)	Lung Air Leak (N)	Infection (N)	Complication Rate (%)
Observation (n = 50)	1	0	0	2.00
Control (n = 50)	2	3	2	14.00
χ^2	-	-	-	4.891
P-value	-	-	-	0.027
Relative risk [c]	-	-	-	0.14 (0.02 - 1.08)

[a] Any complication refers to the occurrence of at least 1 complication event.

[b] Group comparisons for overall complication rates were performed using the χ^2 test.

[c] Relative risk and 95% CI were calculated based on overall complication rates in the observation and control groups.

invasion, whereas HFOV ensures a stable and unobstructed airway, promotes secretion clearance, and reduces infection risk associated with secretion retention (26, 27).

This study also has several novel and clinically relevant aspects. Although the combination of HFOV and PS therapy is well established, our work extends existing evidence by focusing on a well-defined subgroup of neonates with early-stage NRDS, defined as radiographic grade I - II disease, treated within the first hours after birth in a real-world NICU setting. Unlike prior trials and meta-analyses that enrolled heterogeneous populations or initiated HFOV at later disease stages, we evaluated early HFOV-assisted surfactant therapy using standardized ventilatory parameters. Notably, improvements in gas exchange were accompanied by clinically meaningful short-term benefits, including shorter durations of mechanical ventilation and hospitalization, as well as lower complication rates, underscoring the practical relevance of this strategy in routine NICU care.

Beyond its novelty, the potential implications of these findings for clinical practice and resource allocation merit consideration. Our results suggest that early HFOV-assisted surfactant therapy may support a more stratified ventilation approach for neonates with early-stage NRDS, complementing existing lung-protective ventilation protocols. Because HFOV was implemented using standard settings within a routine NICU environment, its scalability appears feasible in centers with established HFOV capability, and the observed reductions in ventilation duration, length of stay, and complications may partially offset associated resource demands.

However, several limitations of this study should be acknowledged. First, the retrospective and nonrandomized design is inherently subject to selection bias and residual confounding. In particular, the lack of multivariable adjustment precluded full control of potential confounders, such as gestational age and Apgar scores, thereby limiting causal inference. Second, the absence of blinding of outcome assessors, due to the retrospective nature of the study and the distinct ventilation modalities applied, may have introduced observer bias, particularly in the assessment of subjective clinical outcomes. Third, this study was conducted at a single center over a limited 2-year period, and the relatively small sample size may restrict the generalizability of the findings to other clinical settings or populations. Finally, although key short-term clinical outcomes were evaluated, long-term respiratory and neurodevelopmental outcomes, such as postdischarge or 6-month respiratory status, were not assessed. Future multicenter prospective studies with larger sample sizes, appropriate multivariable adjustment, and extended follow-up are warranted to further validate these findings.

5.1. Conclusions

High-frequency oscillatory ventilation-assisted PS therapy significantly improves blood gas parameters, shortens the duration of mechanical ventilation and hospitalization, and reduces complication rates in neonates with NRDS, demonstrating considerable clinical value.

Supplementary Material

Supplementary material(s) is available here [To read supplementary materials, please refer to the journal website and open PDF/HTML].

Footnotes

AI Use Disclosure: The authors declare that no generative AI tools were used in the creation of this article.

Authors' Contribution: M. C. contributed to study design and data collection. H. W. contributed to data analysis. W. Z. contributed to writing.

Conflict of Interests Statement: The authors declare no conflict of interest.

Data Availability: The dataset presented in the study is available on request from the corresponding author during submission or after publication.

Ethical Approval: The study was approved by the Ethics Committee of Inner Mongolia Autonomous Region People's Hospital (No. IMARP2022305).

Funding/Support: This study was financially supported by the Public Hospital Research Joint Fund Science and Technology Project (No. 2023GLLHOO81) and the Health Science and Technology Plan Project of Inner Mongolia Autonomous Region (No. 202202040).

Informed Consent: Written informed consent obtained from parents or legal guardians.

References

1. Sweet DG, Carnielli VP, Greisen G, Hallman M, Klebermass-Schrehof K, Ozek E, et al. European Consensus Guidelines on the Management of Respiratory Distress Syndrome: 2022 Update. *Neonatology*. 2023;**120**(1):3-23. [PubMed ID: 36863329]. [PubMed Central ID: PMC10064400]. https://doi.org/10.1159/000528914.
2. De Luca D, Tingay DG, van Kaam AH, Courtney SE, Kneyber MCJ, Tissieres P, et al. Epidemiology of Neonatal Acute Respiratory Distress Syndrome: Prospective, Multicenter, International Cohort Study. *Pediatr Crit Care Med*. 2022;**23**(7):524-34. [PubMed ID: 35543390]. https://doi.org/10.1097/PCC.0000000000002961.
3. Ruegger CM, Owen LS, Davis PG. Nasal Intermittent Positive Pressure Ventilation for Neonatal Respiratory Distress Syndrome. *Clin Perinatol*. 2021;**48**(4):725-44. [PubMed ID: 34774206]. https://doi.org/10.1016/j.clp.2021.07.004.
4. Zha J, Yu YJ, Li GR, Wang SC, Qiao SG, Wang C, et al. Lung protection effect of EIT-based individualized protective ventilation strategy in patients with partial pulmonary resection. *Eur Rev Med Pharmacol Sci*. 2023;**27**(12):5459-67. [PubMed ID: 37401282]. https://doi.org/10.26355/eurrev_202306_32782.
5. Vizzoca A, Lucarini G, Tognoni E, Tognarelli S, Ricotti L, Gherardini L, et al. Erythro-Magneto-HA-Virosome: A Bio-Inspired Drug Delivery System for Active Targeting of Drugs in the Lungs. *Int J Mol Sci*. 2022;**23**(17). [PubMed ID: 36077300]. [PubMed Central ID: PMC9455992]. https://doi.org/10.3390/ijms23179893.
6. Zhu X, Qi H, Feng Z, Shi Y, De Luca D, Nasal Oscillation Post-Extubation Study G. Noninvasive High-Frequency Oscillatory Ventilation vs Nasal Continuous Positive Airway Pressure vs Nasal Intermittent Positive Pressure Ventilation as Postextubation Support for Preterm Neonates in China: A Randomized Clinical Trial. *JAMA Pediatr*. 2022;**176**(6):551-9. [PubMed ID: 35467744]. [PubMed Central ID: PMC9039831]. https://doi.org/10.1001/jamapediatrics.2022.0710.
7. Junqueira FMD, Nadal JAH, Brandao MB, Nogueira RJN, de Souza TH. High-frequency oscillatory ventilation in children: A systematic review and meta-analysis. *Pediatr Pulmonol*. 2021;**56**(7):1872-88. [PubMed ID: 33902159]. https://doi.org/10.1002/ppul.25428.
8. Reynolds P, Bustani P, Darby C, Fernandez Alvarez JR, Fox G, Jones S, et al. Less-Invasive Surfactant Administration for Neonatal Respiratory Distress Syndrome: A Consensus Guideline. *Neonatology*. 2021;**118**(5):586-92. [PubMed ID: 34515188]. https://doi.org/10.1159/000518396.
9. Silveira RC, Panceri C, Munoz NP, Carvalho MB, Fraga AC, Procianoy RS. Less invasive surfactant administration versus intubation-surfactant-extubation in the treatment of neonatal respiratory distress syndrome: a systematic review and meta-analyses. *J Pediatr (Rio J)*. 2024;**100**(1):8-24. [PubMed ID: 37353207]. [PubMed Central ID: PMC10751720]. https://doi.org/10.1016/j.jped.2023.05.008.
10. Wang X, Zhang C, Zou N, Chen Q, Wang C, Zhou X, et al. Lipocalin-2 silencing suppresses inflammation and oxidative stress of acute respiratory distress syndrome by ferroptosis via inhibition of MAPK/ERK pathway in neonatal mice. *Bioengineered*. 2022;**13**(1):508-20. [PubMed ID: 34969358]. [PubMed Central ID: PMC8805876]. https://doi.org/10.1080/21655979.2021.2009970.
11. Li J, Chen L, Shi Y. Nasal high-frequency oscillatory ventilation versus nasal continuous positive airway pressure as primary respiratory support strategies for respiratory distress syndrome in preterm infants: a systematic review and meta-analysis. *Eur J Pediatr*. 2022;**181**(1):215-23. [PubMed ID: 34254173]. https://doi.org/10.1007/s00431-021-04190-0.
12. Cools F, Offringa M, Askie LM. Elective high frequency oscillatory ventilation versus conventional ventilation for acute pulmonary dysfunction in preterm infants. *Cochrane Database Syst Rev*. 2015;**2015**(3). CD000104. [PubMed ID: 25785789]. [PubMed Central ID: PMC10711725]. https://doi.org/10.1002/14651858.CD000104.pub4.
13. Qiao JY, Li YZ, Wang HY, Zhang SD. [A Meta analysis of the efficacy of high-frequency oscillatory ventilation versus conventional mechanical ventilation for treating pediatric acute respiratory distress syndrome]. *Zhongguo Dang Dai Er Ke Za Zhi*. 2017;**19**(4):430-5. chinease. [PubMed ID: 28407831]. [PubMed Central ID: PMC7389656]. https://doi.org/10.7499/j.issn.1008-8830.2017.04.014.
14. Zheng YR, Lei YQ, Liu JF, Wu HL, Xu N, Huang ST, et al. Effect of High-Frequency Oscillatory Ventilation Combined With Pulmonary Surfactant in the Treatment of Acute Respiratory Distress Syndrome After Cardiac Surgery: A Prospective Randomised Controlled Trial. *Front Cardiovasc Med*. 2021;**8**:675213. [PubMed ID: 34368243]. [PubMed Central ID: PMC8339213]. https://doi.org/10.3389/fcvm.2021.675213.
15. Wang TY, Zhu Y, Yin JL, Zhao LY, Wang HJ, Xiao CW, et al. The effect of high-frequency oscillatory ventilator combined with pulmonary surfactant in the treatment of neonatal respiratory distress syndrome. *Medicine (Baltimore)*. 2022;**101**(32). e29940. [PubMed ID: 35960117]. [PubMed Central ID: PMC9371548]. https://doi.org/10.1097/MD.0000000000029940.
16. Choommongkol V, Punturee K, Klumphu P, Rattanaburi P, Meepowpan P, Suttiarporn P. Microwave-Assisted Extraction of Anticancer Flavonoid, 2',4'-Dihydroxy-6'-methoxy-3',5'-dimethyl Chalcone (DMC), Rich Extract from Syzygium nervosum Fruits. *Molecules*. 2022;**27**(4). [PubMed ID: 35209190]. [PubMed Central ID: PMC8877704]. https://doi.org/10.3390/molecules27041397.
17. Wang K, Zhou X, Gao S, Li F, Ju R. Noninvasive high-frequency oscillatory ventilation versus nasal intermittent positive pressure ventilation for preterm infants as an extubation support: A systematic review and meta-analysis. *Pediatr Pulmonol*. 2023;**58**(3):704-11. [PubMed ID: 36372443]. https://doi.org/10.1002/ppul.26244.
18. Yang HB, Pierro A, Kim HY. Comparison of conventional mechanical ventilation and high-frequency oscillatory ventilation in congenital diaphragmatic hernias: a systematic review and meta-analysis. *Sci*

Rep. 2023;**13**(1):16136. [PubMed ID: 37752154]. [PubMed Central ID: PMC10522688]. https://doi.org/10.1038/s41598-023-42344-2.

19. Liu K, Chen L, Xiong J, Xie S, Hu Y, Shi Y. HFOV vs CMV for neonates with moderate-to-severe perinatal onset acute respiratory distress syndrome (NARDS): a propensity score analysis. *Eur J Pediatr*. 2021;**180**(7):2155-64. [PubMed ID: 33638098]. [PubMed Central ID: PMC7910198]. https://doi.org/10.1007/s00431-021-03953-z.
20. Orlandin EAS, Iwashita-Lages T, Oharomari-Junior LK, Tome MR, Zinher MT, Dias SO, et al. Volume-targeted on high-frequency oscillatory ventilation in preterm infants: a systematic review. *J Pediatr (Rio J)*. 2025;**101**(3):332-40. [PubMed ID: 40074210]. [PubMed Central ID: PMC12039505]. https://doi.org/10.1016/j.jped.2025.01.012.
21. Phattraprayoon N, Ho JJ, Fiander M, Priyadarshi M. High-frequency oscillatory ventilation versus conventional ventilation for infants with severe pulmonary dysfunction born at or near term. *Cochrane Database Syst Rev*. 2025;**11**(11). CD002974. [PubMed ID: 41216897]. [PubMed Central ID: PMC12604084]. https://doi.org/10.1002/14651858.CD002974.pub3.
22. Solis-Garcia G, Ramos-Navarro C, Gonzalez-Pacheco N, Sanchez-Luna M. Lung protection strategy with high-frequency oscillatory ventilation improves respiratory outcomes at two years in preterm respiratory distress syndrome: a before and after, quality improvement study. *J Matern Fetal Neonatal Med*. 2022;**35**(26):10698-705. [PubMed ID: 36521851]. https://doi.org/10.1080/14767058.2022.2155040.
23. Dogan S, Paulus M, Surmeier G, Foryt K, Bragelmann K, Tolan M. Nondestructive Compression and Fluidization of Phospholipid Monolayers by Gaseous and Aerolized Perfluorocarbons: Promising Substances for Lung Surfactant Treatment. *Langmuir*. 2022;**38**(21):6690-9. [PubMed ID: 35588471]. https://doi.org/10.1021/acs.langmuir.2c00617.
24. Tan YX, Li SJ, Li HT, Yin XJ, Cheng B, Guo JL, et al. Role of surfactant protein C in neonatal genetic disorders of the surfactant system: A case report. *Medicine (Baltimore)*. 2021;**100**(50). e28201. [PubMed ID: 34918679]. [PubMed Central ID: PMC8677979]. https://doi.org/10.1097/MD.0000000000028201.
25. Zheng YR, Lin SH, Chen YK, Cao H, Chen Q. Rescue high-frequency oscillatory ventilation combined with intermittent mandatory ventilation for infants with acute respiratory distress syndrome after congenital heart surgery. *Cardiol Young*. 2023;**33**(7):1165-71. [PubMed ID: 35912615]. https://doi.org/10.1017/S1047951122002396.
26. Dilday J, Leon D, Kuza CM. A review of the utility of high-frequency oscillatory ventilation in burn and trauma ICU patients. *Curr Opin Anaesthesiol*. 2023;**36**(2):126-31. [PubMed ID: 36729001]. https://doi.org/10.1097/ACO.0000000000001228.
27. Pioselli B, Salomone F, Mazzola G, Amidani D, Sgarbi E, Amadei F, et al. Pulmonary Surfactant: A Unique Biomaterial with Life-saving Therapeutic Applications. *Curr Med Chem*. 2022;**29**(3):526-90. [PubMed ID: 34525915]. https://doi.org/10.2174/0929867328666210825110421.