



NEW APPROACHES IN THE MANAGEMENT OF RESPIRATORY DISTRESS SYNDROME IN PRETERM INFANTS: A NARRATIVE REVIEW

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NARRATIVE REVIEW

ABSTRACT

Respiratory distress syndrome (RDS) remains one of the leading causes of neonatal morbidity and mortality among preterm newborns, particularly due to pulmonary immaturity and surfactant deficiency. Over recent decades, novel therapeutic strategies have contributed to reducing the need for invasive mechanical ventilation, minimizing lung injury, and improving neonatal outcomes. The present study aimed to analyze new approaches related to the management of RDS in preterm infants, with emphasis on noninvasive respiratory support, surfactant therapy, minimally invasive administration techniques, and protective ventilation strategies. This study consists of a Narrative Literature Review conducted through searches in databases including PubMed, Scopus, Web of Science, SciELO, and ScienceDirect, covering publications from 2016 to 2026. The research question was developed according to the PICO strategy, considering preterm newborns with RDS, contemporary therapeutic approaches, and the context of neonatal intensive care. The findings demonstrate that early nasal CPAP, LISA/MIST techniques, and volume-targeted ventilation have assumed a central role in reducing intubation rates, exposure to invasive ventilation, and respiratory complications. Furthermore, controlled oxygenation strategies, continuous monitoring, and emerging therapies such as aerosolized surfactant indicate promising perspectives. Nevertheless, challenges related to protocol standardization, multiprofessional training, technological availability, and equitable access still persist. It is concluded that the contemporary management of RDS in preterm infants is moving toward increasingly individualized, protective, and less invasive approaches.

Keywords: Prematurity; Respiratory Distress Syndrome; Pulmonary Surfactant; Noninvasive Ventilation; Neonatal Intensive Care.



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1- INTRODUCTION

Respiratory distress syndrome (RDS) represents one of the major complications associated with prematurity and remains linked to high neonatal morbidity, particularly among newborns with lower gestational age. Its pathophysiology is related to quantitative and functional surfactant deficiency, structural alveolar immaturity, and reduced pulmonary compliance, factors that contribute to atelectasis, hypoxemia, and increased respiratory effort during the first hours of life (SWEET *et al.*, 2023; NG; SHAH, 2021).

Historically, the introduction of exogenous surfactant therapy and neonatal mechanical ventilation represented a milestone in reducing mortality associated with RDS. However, the recognition of the adverse effects related to prolonged invasive ventilation, including barotrauma, volutrauma, pulmonary inflammation, and increased risk of bronchopulmonary dysplasia, led to substantial reformulation of neonatal respiratory care protocols over recent decades (DARGAVILLE *et al.*, 2021; TANA *et al.*, 2023).

Within this context, contemporary strategies have increasingly prioritized less invasive interventions, such as early nasal CPAP, noninvasive ventilation, and minimally invasive surfactant administration. These approaches aim to preserve spontaneous breathing, reduce the need for endotracheal intubation, and limit the exposure of the immature lung to potentially harmful pressures and volumes (SWEET *et al.*, 2023; BHANDARI *et al.*, 2023).

In addition to strategies already incorporated into clinical practice, new therapeutic possibilities have been investigated, including aerosolized surfactant, improved ventilatory interfaces, continuous respiratory monitoring, and more protective ventilatory modes. Although promising, these technologies still require clinical validation, technical standardization, and cost-effectiveness assessment, particularly across different neonatal care settings (BRASHER *et al.*, 2021; JARDINE *et al.*, 2022).

Given this scenario, the present study aimed to analyze new approaches related to the management of respiratory distress syndrome in preterm infants, emphasizing contemporary ventilatory strategies, surfactant therapies, noninvasive respiratory



support methods, and emerging therapeutic perspectives in modern neonatology.

2- METHOD

This study consists of a Narrative Literature Review, a methodological approach considered appropriate for gathering, interpreting, and critically discussing scientific evidence on broad, complex, and constantly evolving topics. This approach allows the integration of clinical guidelines, systematic reviews, clinical trials, observational studies, and specialized consensus statements, thereby promoting a comprehensive understanding of novel strategies in the respiratory management of preterm newborns with RDS (TANA *et al.*, 2023; SWEET *et al.*, 2023).

The research question was developed based on the PICO strategy. The population (P) consisted of preterm newborns diagnosed with respiratory distress syndrome; the phenomenon of interest (I) included novel therapeutic approaches and contemporary ventilatory strategies; and the context (Co) encompassed neonatal intensive care units and specialized neonatology services. Accordingly, the following guiding research question was established: what are the main contemporary approaches used in the management of respiratory distress syndrome in preterm newborns and what are their impacts on neonatal outcomes?

The search strategy was planned using the PubMed, Scopus, Web of Science, SciELO, and ScienceDirect databases, employing descriptors and keywords such as “Respiratory Distress Syndrome,” “Preterm Infant,” “Surfactant Therapy,” “Noninvasive Ventilation,” “Continuous Positive Airway Pressure,” “Less Invasive Surfactant Administration,” and “Neonatal Intensive Care,” combined through the Boolean operators AND and OR. Studies published between 2016 and 2026 in Portuguese, English, and Spanish were considered eligible. Publications directly related to neonatal respiratory management in preterm infants with RDS were included, whereas editorials, letters to the editor, exclusively experimental animal studies, and studies unrelated to the neonatal context were excluded.

3- RESULTS



The analyzed studies demonstrate that the contemporary management of RDS in preterm infants has increasingly prioritized less invasive strategies aimed at reducing lung injury associated with intubation and invasive mechanical ventilation. Early use of nasal CPAP, particularly immediately after birth or during the first hours of life, is recommended for preterm infants with spontaneous breathing, as it contributes to alveolar stabilization, improvement of functional residual capacity, and reduction in the need for intubation (SWEET *et al.*, 2023; NG; SHAH, 2021; HO; SUBRAMANIAM; DAVIS, 2020).

Surfactant administration remains a central intervention in the treatment of RDS, especially in newborns who present progressive increases in oxygen requirements despite noninvasive respiratory support. However, the method of administration has evolved, with increasing emphasis on minimally invasive techniques such as LISA and MIST, which allow surfactant delivery through a thin catheter while the newborn maintains spontaneous breathing under CPAP support (DARGAVILLE *et al.*, 2021; TANA *et al.*, 2023; BHANDARI *et al.*, 2023; RÜEGGER; OWEN; DAVIS, 2021).

Another relevant finding concerns the individualization of neonatal ventilatory strategies. In preterm infants requiring mechanical ventilation, volume-targeted or volume-guarantee modes have been associated with reductions in adverse outcomes when compared with pressure-limited ventilation, particularly by decreasing excessive tidal volume fluctuations and reducing the risk of ventilator-induced lung injury (KLINGENBERG *et al.*, 2017; TANA *et al.*, 2023; BOEL *et al.*, 2022).

Overall, the findings suggest that new approaches in the management of respiratory distress syndrome in preterm infants have promoted significant reductions in neonatal respiratory complications and improvements in clinical outcomes in neonatal intensive care. Nevertheless, the literature also highlights challenges related to the uniform implementation of these strategies, the need for multiprofessional training, and inequalities in technological access among different neonatal care services (CRESI *et al.*, 2023; ZHANG *et al.*, 2022; BUYUKTIRYAKI *et al.*, 2020). In this context, aiming to synthesize the main studies analyzed, their clinical findings, and the contemporary therapeutic approaches identified in the literature, a summary table presenting the most relevant evidence from this narrative review will be provided



below.

Table 1. Summary of the Main Studies on Contemporary Approaches in the Management of Respiratory Distress Syndrome in Preterm Infants

Authors/ Year	Study Design	Main Objective	Therapeutic/ Ventilatory Approach	Main Findings	Clinical Implications
Sweet et al. (2023)	International Consensus Guidelines	To update evidence-based recommendations for the management of neonatal RDS	Early CPAP, surfactant therapy, protective ventilation	Early noninvasive respiratory support reduces invasive ventilation exposure and improves respiratory outcomes	Consolidates standardized evidence-based neonatal respiratory care
Ng and Shah (2021)	Clinical Guidelines	To establish recommendations for surfactant replacement therapy in neonates	Surfactant replacement therapy	Surfactant administration remains essential for moderate and severe RDS management	Supports early and individualized surfactant administration
Dargaville et al. (2021)	Randomized Clinical Trial	To evaluate minimally invasive surfactant therapy in preterm infants	MIST/LISA techniques	Minimally invasive surfactant administration reduced mechanical ventilation exposure	Reinforces less invasive respiratory management strategies
Ho, Subramaniyam and Davis (2020)	Cochrane Systematic Review	To assess the effectiveness of CPAP in preterm infants with RDS	Nasal CPAP	CPAP reduced intubation rates and respiratory complications	Supports early CPAP as first-line respiratory support
Klingenberg et al. (2017)	Cochrane Systematic Review	To compare volume-targeted versus pressure-limited ventilation	Volume-targeted ventilation	Volume-targeted ventilation reduced lung injury and ventilatory instability	Encourages protective mechanical ventilation practices
Tana et al. (2023)	Narrative Review	To discuss evidence-based respiratory management in preterm infants	Noninvasive ventilation and individualized respiratory care	Personalized respiratory support improves pulmonary outcomes and reduces complications	Highlights the importance of individualized neonatal respiratory strategies
Brasher et al. (2021)	Review Article	To evaluate aerosolized surfactant therapy in preterm infants	Aerosolized surfactant	Aerosolized surfactant demonstrated feasibility and potential for less invasive administration	Suggests future perspectives for noninvasive surfactant delivery
Jardine et al. (2022)	Clinical Trial	To investigate aerosolized surfactant	Aerosolized surfactant administration	Initial results demonstrated safety	Supports further investigation of



		therapy in neonatal RDS		and clinical feasibility	aerosolized surfactant
Rüegger, Owen and Davis (2021)	Review Article	To evaluate nasal intermittent positive pressure ventilation in neonatal RDS	NIPPV	NIPPV may reduce extubation failure and improve respiratory stability	Expands noninvasive ventilatory support alternatives
Cresi <i>et al.</i> (2023)	Randomized Clinical Trial	To compare nasal CPAP and high-flow nasal cannula in preterm infants	CPAP versus heated humidified high-flow therapy	Both methods demonstrated respiratory support efficacy, with distinct tolerability profiles	Supports individualized selection of noninvasive respiratory support
Zhang <i>et al.</i> (2022)	Multicenter Study Protocol	To compare CPAP and NIPPV before minimally invasive surfactant administration	CPAP and NIPPV associated with LISA/MIST	Combined noninvasive approaches may optimize respiratory stabilization	Indicates growing integration of multimodal noninvasive strategies
Buyuktiryaki <i>et al.</i> (2020)	Retrospective Comparative Study	To compare different noninvasive ventilation strategies in very low birth weight infants	Noninvasive ventilation strategies	Distinct noninvasive modalities demonstrated effectiveness in respiratory stabilization	Reinforces the relevance of individualized ventilatory support

Source: Prepared by the authors (2026).

4- DISCUSSION

The evolution of the management of respiratory distress syndrome in preterm infants reflects important scientific and technological advances in contemporary neonatology. The transition from a care model centered on invasive ventilation toward less aggressive strategies demonstrates a paradigm shift guided by lung protection, preservation of spontaneous breathing, and reduction of both short- and long-term respiratory complications (SWEET *et al.*, 2023; TANA *et al.*, 2023).

Although invasive mechanical ventilation remains indispensable in severe cases of respiratory failure, it is associated with significant risks when used for prolonged periods or with inappropriate ventilatory parameters. The preterm lung is particularly vulnerable to injury caused by excessive pressure, volume, and oxygen exposure, reinforcing the need for carefully adjusted and continuously monitored ventilatory



strategies (KLINGENBERG *et al.*, 2017; TANA *et al.*, 2023).

Early nasal CPAP occupies a central role in the current management of RDS, especially because it promotes alveolar recruitment without the immediate need for intubation. International guidelines recommend noninvasive respiratory support from the first minutes of life in preterm infants with spontaneous breathing, combined with continuous assessment of surfactant requirements according to clinical progression and oxygen demand (SWEET *et al.*, 2023; NG; SHAH, 2021).

LISA and MIST techniques represent one of the major innovations in the contemporary treatment of RDS. By allowing surfactant administration without prolonged invasive mechanical ventilation, these strategies align with the principle of minimizing pulmonary trauma while preserving the respiratory physiology of preterm infants. Clinical trials demonstrate that minimally invasive surfactant therapy may reduce the need for intubation and mechanical ventilation, although its impact on composite outcomes such as death or bronchopulmonary dysplasia should be interpreted according to patient population, gestational age, and protocol characteristics (DARGAVILLE *et al.*, 2021; BHANDARI *et al.*, 2023).

Controlled oxygen therapy also represents an essential component of neonatal respiratory care. Insufficient oxygen exposure may worsen hypoxemia and clinical instability, whereas hyperoxia is associated with oxidative stress and complications such as retinopathy of prematurity and pulmonary injury. Therefore, target oxygen saturation protocols and continuous monitoring have been incorporated as indispensable components of care for preterm infants with RDS (SWEET *et al.*, 2023; TANA *et al.*, 2023).

Emerging approaches, such as aerosolized surfactant, have attracted interest because they offer the possibility of an even less invasive administration method without the need for tracheal catheterization. Initial studies indicate feasibility and safety in specific settings; however, important limitations still exist regarding pulmonary deposition, respiratory synchronization, optimal dosing, nebulizer type, and confirmation of efficacy in larger clinical trials (BRASHER *et al.*, 2021; JARDINE *et al.*, 2022).

Despite the advances observed, the implementation of these strategies does not occur uniformly across different neonatal care services. The safe adoption of early CPAP,



LISA/MIST, protective ventilation, and advanced monitoring requires trained teams, clear institutional protocols, adequate equipment availability, and a healthcare culture focused on neonatal quality and safety. In resource-limited settings, inequalities in access may compromise the incorporation of the best available evidence into clinical practice (BHANDARI *et al.*, 2023; NG; SHAH, 2021).

Finally, the future of RDS management in preterm infants is expected to be marked by increasingly personalized interventions, real-time monitoring, and the integration of technologies capable of supporting clinical decision-making. Nevertheless, the consolidation of these innovations will depend on the production of robust scientific evidence, cost-effectiveness evaluation, continuous professional training, and the equitable expansion of access to neonatal technologies, ensuring that scientific progress translates into meaningful improvements in outcomes for preterm newborns (TANA *et al.*, 2023; SWEET *et al.*, 2023).

5- CONCLUSION

The new approaches related to the management of respiratory distress syndrome in preterm infants represent important advances in contemporary neonatal care. Less invasive strategies, modern surfactant therapies, and protective ventilatory methods have contributed to reducing exposure to invasive mechanical ventilation and improving the quality of respiratory care in neonatal intensive care units.

The analyzed studies demonstrate that interventions such as early nasal CPAP, minimally invasive surfactant administration, and volume-targeted ventilation promote a more physiological and protective approach to the preterm lung. These strategies reinforce the current trend toward individualized respiratory support, with emphasis on the prevention of pulmonary injury and the improvement of neonatal outcomes.

Nevertheless, challenges related to team training, protocol standardization, technological availability, and inequalities in access among different healthcare services still persist. Therefore, the incorporation of new strategies should be accompanied by multiprofessional training, continuous outcome assessment, and adaptation to institutional realities.



It is concluded that the contemporary management of RDS in preterm infants is moving toward increasingly individualized, less invasive, and technologically integrated approaches. The consolidation of these strategies will depend on consistent scientific evidence, investments in neonatal infrastructure, and commitment to safety, quality of care, and equity in the management of preterm newborns.

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