International Journal of Science and Research (IJSR)
ISSN: 2319-7064
Impact Factor 2024: 7.101

# Case Review: Managing Neonatal Pulmonary Hypertension in Barranquilla, Colombia

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**Abstract:** ***Pulmonary hypertension in neonates is a life-threatening condition that significantly contributes to neonatal morbidity and mortality, particularly in preterm newborns or those with underlying conditions. This study reviews the combination therapy of high-frequency oscillatory ventilation (HFOV) and nitric oxide (NO) through the analysis of four clinical cases from Barranquilla, Colombia. The findings highlight the potential of this synergistic approach in improving oxygenation and reducing pulmonary arterial pressure. The review underscores the importance of early, multidisciplinary intervention in enhancing clinical outcomes for affected neonates.***

**Keywords:** Pulmonary hypertension, Nitric Oxide, Pulmonary surfactant, Neonatal intensive care, Respiratory distress, Preterm infants

## 1. Introduction

Pulmonary hypertension in neonates is a critical condition characterized by an abnormal increase in pulmonary artery pressure, with potentially serious consequences and high mortality. This disorder is more common in preterm infants and in those with associated conditions such as perinatal asphyxia and bronchopulmonary dysplasia [1, 2, 3]. Early and effective management of pulmonary hypertension is essential to improve clinical outcomes and survival of these patients. Pulmonary hypertension (PH) in neonates presents a varied epidemiology, in term newborns it may occur in approximately 1% to 5%; however, this percentage may be higher in relation to risk conditions such as perinatal asphyxia and congenital cardiac malformations. The prevalence of PH is significantly higher in preterm neonates, with figures that can range from 10% to 30% due to factors such as pulmonary immaturity and bronchopulmonary dysplasia [1, 4, 5].

The purpose of this study is to evaluate the effectiveness of combining HFOV and nitric oxide therapy in managing neonatal pulmonary hypertension through case analysis.

High-frequency oscillatory ventilation (HFOV) has established itself as a key strategy in the management of neonatal respiratory failure. This approach allows for more efficient ventilation with lower air volumes, reducing the risk of lung injury induced by conventional ventilation [1]. HFVO works by generating more uniform pressures in the alveoli, which minimizes barotrauma and improves oxygenation and carbon dioxide removal [2]. In turn, nitric oxide (NO), a potent vasodilator specific for the pulmonary vascular bed, has been used in the treatment of persistent pulmonary hypertension. Its action is based on the stimulation of soluble guanylate cyclase, which increases cyclic GMP levels and consequently causes relaxation of vascular smooth muscle [2]. The combination of HFVO with nitric oxide administration may potentiate these effects by reducing pulmonary vascular resistance and improving perfusion in ventilated areas, which favors better oxygenation [4].

The synergy between HFVO and NO translates into a double benefit: while HFVO optimizes respiratory mechanics and reduces intrathoracic pressure, NO promotes vasodilatation in the pulmonary bed, thus contributing to the decrease in pulmonary arterial pressure [2, 3, 5]. This article reviews the current evidence on high-frequency ventilation with nitric oxide in the early management of pulmonary hypertension in neonates, analyzing the physiological mechanisms, clinical indications and the most relevant results in neonatal practice. Through this review, we seek to provide a clearer understanding of this therapeutic strategy and its potential to improve outcomes in this population.

This study highlights the need for timely and advanced interventions, offering insights into practical therapeutic strategies that may significantly reduce neonatal mortality associated with pulmonary hypertension.

## 2. Methodology

The methodology of this case report consists of a thorough analysis of the patient's clinical history during the prenatal period, complemented by the approaches of each medical specialty involved in the treatment. In addition, a relevant literature review is performed using databases such as PubMed, Medline and Embase, to contextualize and explain the findings obtained.

## 3. Description of cases

**Case #1:**
Preterm newborn of 32 weeks by Ballard, born in second level medical center by cesarean section motivated by unsatisfactory fetal status (fetal bradycardia) and preterm labor syndrome, with nasal flaring, marked intercostal and subcostal pulls, audible whine (Silverman 5/10) to which they

indicated referral to the Neonatal Intensive Care Unit, INSURE technique is performed there and continues with Invasive Mechanical Ventilation with high parameters. Critically ill patient with mean airway pressure (MAP) >10, arterial blood gases, respiratory acidemia, PaFi 202, early transthoracic echocardiogram was made, which showed pulmonary pressure estimated at 70 mmhg, managed with High Frequency Ventilation + Nitric Oxide. Additionally, she presented radiographic findings suggestive of Hyaline Membrane Disease with surfactant consumption, requiring an additional dose of exogenous pulmonary surfactant. The control transthoracic echocardiogram showed pulmonary pressure estimated at 52 mmhg, arterial blood gases showed respiratory alkalosis, so weaning of ventilatory parameters was started until High Frequency Ventilation was suspended and she continued with Nitric Oxide management until a control transthoracic echocardiogram was performed with pulmonary pressure estimated at 25 mmhg and management was suspended.

**Case #2:**
Preterm male newborn, 36 weeks by Ballard, born in a second level medical center on the day of cesarean section due to cephalopelvic disproportion and mother with preeclampsia without severity criteria. Born in apnea, cyanotic, requiring positive pressure ventilation, he was referred to the Neonatal Intensive Care Unit, where he was admitted with marked intercostal and subcostal pulls, audible moaning without phonendoscope and nasal flaring, for which Invasive Mechanical Ventilation was indicated. Chest X-rays revealed bilateral alveolar opacities consistent with pneumonia and surfactant depletion, and a dose of exogenous pulmonary surfactant was administered. Critical patient with mean airway pressure >10, PaFi 200, with high ventilatory parameters. Arterial blood gas analysis reported severe metabolic acidemia. A transthoracic echocardiogram was performed, which showed severe hypertension of 60 mmhg, and once the blood pressure was stabilized, high frequency ventilation + nitric oxide was started, after which a control transthoracic echocardiogram was performed, which showed mild to moderate hypertension of 35 mmhg, and it was decided to discontinue high frequency ventilation. A new control transthoracic echocardiogram was made, which showed mild pulmonary hypertension, and was evaluated by the pediatric cardiology service, which indicated a decrease in parameters according to tolerance and control according to clinical evolution.

**Case #3:**
Preterm male newborn of 35 weeks by Ballard, born by cesarean section due to non-reassuring fetal condition, with audible whimpering and subcostal pulls (Silverman 5/10 points) and therefore admitted to the Neonatal Intensive Care Unit, initial management with noninvasive nasal mechanical ventilation was performed, However, he presented marked deterioration of ventilatory mechanics and radiological evidence of low lung volume, making it necessary to initiate Invasive Mechanical Ventilation with high ventilatory parameters and administration of doses of Exogenous Pulmonary Surfactant for alveolar recruitment. The patient had a mean airway pressure of 11.2 and a PaFi of 201, with a blood gas report indicating severe respiratory acidosis. Early transthoracic echocardiogram was performed which showed pulmonary pressure estimated at 60 mmhg, managed with high frequency ventilation and vasodilator treatment with nitric oxide for 36 hours after which transthoracic echocardiogram control was performed which showed pulmonary pressure estimated at 25 mmhg.

**Case #4:**
Female newborn at term 37 weeks by Ballard, born by cesarean section motivated by preeclampsia with severity criteria for neurohypertensive symptoms, presenting signs of respiratory distress by nasal flaring, intercostal and mild subcostal pulls, and audible moaning with phonendoscope (Silverman 4/10 points) requiring admission to the Neonatal Intensive Care Unit, Initial management with oxygen support by nasal cannula and subsequent noninvasive nasal mechanical ventilation without improvement, which required invasive mechanical ventilation with high parameters and doses of exogenous pulmonary surfactant due to radiological evidence of pneumonia with consumption of pulmonary surfactant. Patient with arterial blood gas report of mixed acidosis, PaFi 205, mean airway pressure (MAP) 10, initial transthoracic echocardiogram was done which showed pulmonary pressure estimated at 50 mmhg so High Frequency Ventilation was started and management with Nitric Oxide for 48 hours, obtaining a control transthoracic echocardiogram which showed pulmonary pressure estimated at 25 mmhg.

## 4. Discussion

PPHN is characterized by elevated pulmonary vascular resistance after birth, causing right-to-left shunting of blood and resulting in severe hypoxemia. Its prevalence is 2 per 1000 live births, affecting mainly term and late preterm infants, although it can also occur in post-term neonates [6,7,8]. It is uncommon in those with very low birth weight, but recent studies indicate an increase in the prevalence of PPHN among extremely preterm infants, with increased risk with decreasing gestational age [9]. Maternal risk factors include obesity, diabetes, advanced age, exposure to selective serotonin reuptake inhibitors (SSRIs), meconium-stained amniotic fluid, premature rupture of membranes, among others [10]. In the four cases analyzed, PPHN was associated with prematurity (Cases 1, 2 and 3), maternal pathologies such as preeclampsia (Cases 2 and 4), and acute fetal compromise (Cases 1 and 3), which is consistent with the literature on conditions affecting cardiorespiratory adaptation at birth. PPHN is associated with three abnormalities in the pulmonary vasculature: underdevelopment, maldevelopment, and maladaptation [10,11,12].

- Underdevelopment: refers to an underdeveloped pulmonary vasculature, as in pulmonary hypoplasia, which elevates pulmonary vascular resistance (PVR) and increases the risk of mortality.
- Maldevelopment: Structurally normal lungs but with alterations such as thickened pulmonary arterioles and excess extracellular matrix, associated with post-term delivery and meconium aspiration syndrome.
- Maladaptation: Adverse perinatal factors, such as perinatal depression and bacterial infections (e.g., group B streptococcus), cause vasoconstriction and hinder PVR reduction after birth [13].

Most newborns with PPHN exhibit respiratory distress within the first 24 hours after birth. In one study, more than half of the infants had low APGAR scores, and almost all required interventions in the delivery room, such as oxygen therapy, bag and mask ventilation, and endotracheal intubation [6].

For diagnosis, patients usually undergo initial tests including pulse oximetry (pre- and postductal oxygen saturation), arterial blood gas analysis, chest radiographs, and evaluation for sepsis. However, definitive diagnosis is usually made by echocardiography, which usually reveals structurally normal cardiac anatomy, but with signs of pulmonary hypertension, such as elevated right ventricular pressure. Right ventricular pressure is estimated by Doppler measurement of the tricuspid regurgitation jet velocity, if present. If regurgitation is not observed, pressure can be assessed qualitatively, for example, through a flattened or displaced ventricular septum. In cases of severe pulmonary hypertension, echocardiography may show a right-to-left shunt through the patent ductus arteriosus or foramen ovale [10,14].

The oxygenation index (OI) is used to assess the severity of hypoxemia, which reflects the degree of right-to-left shunt. The OI guides the timing of interventions, such as inhaled nitric oxide (iNO) or extracorporeal membrane oxygenation (ECMO) support [15].

Treatment for persistent pulmonary hypertension is aimed at correcting all those factors that may favor vasoconstriction such as hypothermia, hypoglycemia, hypocalcemia, anemia and hypovolemia. [16]. So its main goal will be to induce improvement in oxygenation and a reduction in pulmonary artery pressure.

The gold standard is inhaled nitric oxide (iNO), a selective pulmonary vasodilator that acts on the pulmonary circulation without affecting systemic arterial pressure. The initial dose is 20 ppm, progressively reducing to 1 ppm when FiO2 is <0.6 [16,17]. Clinical trials have shown that NOi improves oxygenation in preterm infants with severe hypoxemia [10,19]. It is essential to avoid abrupt discontinuation of treatment to prevent rebound pulmonary hypertension [18,19].

Combining HFOV, nitric oxide, and exogenous pulmonary surfactant effectively improves oxygenation and lowers pulmonary pressure. HFOV facilitates alveolar recruitment, while NOi improves pulmonary perfusion without compromising systemic hemodynamics [20, 21]. In cases 1 and 3, this strategy allowed discontinuation of HFOV after 24 to 48 hours by significantly reducing pulmonary pressures. In cases 2 and 4, exogenous pulmonary surfactant was crucial in neonates with pneumonia or hyaline membrane disease, aiding in alveolar recruitment and stabilizing respiratory mechanics [20, 21, 22].

The clinical course varied according to gestational age and perinatal conditions. In case 4 (term newborn), resolution of PPHN was more rapid due to better pulmonary maturation. In contrast, in case 2 (preterm newborn with pneumonia and maternal preeclampsia), the clinical course was more prolonged.

## 5. Conclusion

Effective management of neonatal pulmonary hypertension requires early, multidisciplinary interventions. The presented cases demonstrate the potential of combining HFOV and nitric oxide therapy to stabilize clinical outcomes. This therapeutic approach offers a pathway to reducing morbidity and mortality in affected neonates, underscoring the importance of vigilance in neonatal care.

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