

## EDITORIAL

# Persistent Pulmonary Hypertension of Newborn (PPHN)

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### Introduction

Persistent pulmonary hypertension of the newborn (PPHN) can occur due to failure of the normal cardiopulmonary transition. Incidence is 2 per 1000 live born term infants, and some degree of pulmonary hypertension complicates the course of more than 10% of all neonates with respiratory failure.<sup>1</sup> It is associated with high mortality and morbidity.

Pulmonary hypertension is a normal and necessary state for the fetus. At birth, with air entering the lungs and the umbilical cord being clamped, the situation is reversed with the Pulmonary vascular resistance (PVR) falling due to vasodilatation of vessels with oxygenation and systemic vascular resistance (SVR) rising due to the elimination of the low-resistance placental circuit. In PPHN this transition is disturbed, resulting in sustained elevation of PVR. PVR exceeds SVR resulting in the right-to-left haemodynamic shunting through the patent foramen ovale and/or ductus arteriosus leading to the vicious cycle of hypoxaemia, further resulting in pulmonary vasoconstriction leading to diminishing pulmonary perfusion and systemic hypoxaemia.<sup>2</sup> The main hallmarks of PPHN include sustained elevation of PVR, abnormal vasoreactivity and structural remodeling of the pulmonary vascular bed.<sup>3</sup> Idiopathic PH is found in 10-20% of all infants with PPHN.<sup>4</sup>

A high index of clinical suspicion is warranted to diagnose PPHN in a baby. The presence of any of the risk factors like Birth asphyxia, Meconium aspiration, Early-onset Sepsis/Pneumonia, Pulmonary hypoplasia due to causes like Congenital diaphragmatic hernia, amniotic fluid leak, oligohydramnios, pleural effusion, maternal drug intake like NSAIDs (Ibuprofen, aspirin, naproxen,

indomethacin) and selective serotonin-reuptack (SSRI), especially fluoxetine, other factors like RDS, hypothermia, hypoglycaemia, polycythaemia, familial occurrence should prompt the diagnosis.<sup>5,6</sup>

### Diagnosis

Affected infants are usually full-term or post-term and are frequently born through meconium-stained amniotic fluid. The infant is either ill in the delivery room itself or illness manifests within the first 12 hours of life. Infants with PPHN may manifest with severe cyanosis, tachypnoea, grunting, nasal flaring, chest retractions, tachycardia, and shock although signs of respiratory distress may be minimal initially.<sup>7</sup> Cardiac examination may reveal prominent precordial impulse, single or narrowly split and accentuated second heart sound and/or a systolic murmur consistent with tricuspid valve regurgitation. Heart failure is usually not seen though hypotension is encountered.<sup>7</sup> Difference in pre and post ductal saturation of >10% in the absence of structural heart disease suggests PPHN.<sup>8</sup> When hyperventilated for 10 minutes, infants with PPHN may show an increase in PaO<sub>2</sub> by >30 mmHg when pH is raised to 7.55.<sup>9</sup> The chest radiograph usually appears normal in asphyxia associated and idiopathic PPHN. Echocardiography remains the gold standard for diagnosing PPHN. Differential diagnosis include cyanotic congenital heart disease (especially obstructed total anomalous pulmonary venous connection) and entities that predispose to PPHN.<sup>10</sup>

### Management

The aim of treatment is to lower pulmonary vascular resistance, maintain systemic blood pressure, reverse right to left shunt, and improve arterial oxygen saturation.<sup>11</sup> For the majority of PPHN

infants treatment frequently includes aggressive support of cardiac function and perfusion, with volume and inotropic agents to enhance cardiac output and systemic O<sub>2</sub> transport. Oxygen is well known as a pulmonary vasodilator and should be started at 100%.<sup>12</sup> Primary treatment of the neonate depends on the underlying disorder. A variety of treatment options includes surfactant, sedation, alkalization, vasodilatation (e.g., inhaled nitric oxide, prostaglandin, milrinone, magnesium sulfate, adenosine, bosentan, sildenafil) and extracorporeal membrane oxygenation (ECMO).<sup>13</sup> Ventilation is crucial for PPHN treatment since it facilitates alveolar recruitment and lung expansion, improving ventilation/perfusion matching.<sup>14</sup> High frequency oscillatory ventilation may be useful in the management of infants who are being considered for treatment with extracorporeal membrane oxygenation (ECMO).<sup>12</sup> The combined use of inhaled nitric oxide (iNO) and high occupancy vehicle (HFOV) has been demonstrated to be more successful than use of iNO or HFOV alone.<sup>7</sup>

However, many developing countries and resource limited centers do not have the funds or the technical expertise required for these expensive therapies.<sup>15</sup> Sildenafil is a potent and selective inhibitor of cGMP-specific phosphodiesterase 5 (PDE5). This isoenzyme metabolizes cGMP which is the second-messenger of NO and a principle mediator of smooth muscle relaxation and vasodilatation. By inhibiting the hydrolytic breakdown of cGMP, sildenafil prolongs the action of cGMP. This results in augmented smooth muscle relaxation and cause pulmonary vasodilatation.<sup>16</sup> Sildenafil decreases pulmonary vascular resistance in pulmonary hypertensive neonate.<sup>17</sup> Fatema et al<sup>18</sup>, Mamun et al<sup>19</sup> and Wadud et al<sup>20</sup> found that sildenafil is very effective in the treatment of PPHN among Bangladeshi neonate. So where nitric oxide facilities are not available, cheap alternative like sildenafil for first line treatment of PPHN Can be effectively used.

### Conclusion

PPHN is a devastating disease affecting neonates with high mortality and morbidity. Resource limited centers do not have the funds or the technical expertise required for these expensive therapies. Proper identification along with alternative and less

expensive treatment leads to better outcome in PPHN in countries with limited resources.

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