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Etiological Profile Of Persitent Pulmonary Hypertension Of Newborn In A Rural Tertiary Care Hospital

Dr. Navaneeth V Swamy, Dr. Mahendrappa K B, Dr. Sanjeev Jamkhandi, Dr. Arpita B Poojary, Dr. Aditi Gaonkar, Dr. Ravipati Rangaswamy Reddy
Adichunchanagiri Institute Of Medical Sciences, B G Nagara, Mandya, Pin- 571448

Abstract
Background
Persistent pulmonary hypertension is severe unresponsive hypoxic respiratory failure which reflects the failure of the transition of fetal to neonatal circulation. It is a common comorbidity in babies with perinatal asphyxia and meconium aspiration syndrome. It is diagnosed clinically based on evidence of hypoxemia associated with cyanosis. However, 2d echocardiogram is done for the diagnosis of pphn. Management includes adequate oxygenation, maintaining blood pressure, avoiding respiratory or metabolic acidosis, pulmonary vasodilator therapy. Immediate care is necessary to prevent mortality, neuro morbidity neurodevelopmental disabilities such as deafness.
Case presentation
The neonates admitted in our nicu for various etiological factors were observed and studied. Babies that were oxygen dependent were further investigated for pphn and 2d echocardiography was done. Prompt diagnosis and medical management has improved these babies and successfully discharged from our nicu. However, among the 5 cases we have reported 1 death.
Conclusion
Timely diagnosis and treatment of pphn can reduce the morbidity and mortality. Sildenafil (1-3mg/kg every 6th hour) is shown to improve oxygenation and reduce mortality. Long term follow up is essential for these infants due to high risk of neurodevelopmental and hearing abnormalities.

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I. Introduction

Persistent Pulmonary Hypertension of the newborn (PPHN) was initially reported by Gersony et al in 1969 as long-term presence in fetal circulation[1]. Nevertheless, Fox and associates reported in 1977 that desaturating newborns with a patent ductus arteriosus or patent foramen ovale detected during cardiac catheterization had right to left shunt in the absence of congenital heart disease[2].

A fetus's higher pulmonary vascular resistance (PVR), which is about twice as high as that of a neonate, is caused by a variety of circumstances, including intrauterine relative hypoxemia. Newborn babies see a reduction in PVR when ventilation, oxygenation, and pulmonary blood flow increase soon after birth. Persistent Pulmonary Hypertension of the Newborn (PPHN) is a dangerous medical disease that arises from a failure of the postnatal decline in PVR[3,4].

Although there are several contributing factors to PPHN, such as maternal and neonatal conditions, Meconium Aspiration Syndrome (MAS) continues to be the most frequent cause of PPHN[4,5]. According to studies, PPHN is associated with a considerable mortality and morbidity rate, which can reach as high as 10–20%, if it is not detected and treated early[3,4]. The Walsh-Sukys study have reported an incidence of 1.9/1000 live births and mortality of 12-29%[6].

Studies have shown that Echocardiography is the gold standard for confirming a diagnosis, and to monitor the efficacy of specific therapeutic measures in PPHN[9-11]. Right-sided pressures and hemodynamic physiology can be inferred by measuring the ductal and foramen ovale shunt direction, the flattening or left-deviation of the interventricular septum, and the tricuspid regurgitation velocity while also measuring the systemic blood pressure[7,8].

Prompt clinical diagnosis confirmed by 2D Echocardiography helps in timely start of medical management which helps in preventing the further complications and eventually death[5]. This review helps in a discussion of Persistent Pulmonary Hypertension (PPHN) cases that were identified based on their etiological profile at our setup and the medical management used.

II. Case Series:

Case-1:

A term female baby was born via Normal Vaginal Delivery with a birth weight of 3kgs. The baby cried after which Bag and Mask ventilation was given. On Day 1 of life, baby had a Downes Score of 4/10. Hence, CPAP was connected with a FiO2 OF 40% and PEEP 5 and IV Antibiotics was started. Later the baby improved, so CPAP was disconnected and was connected to Oxygen via prongs on Day 2 of life.

On Day 2 of life, the baby had seizures and was loaded with Inj. Phenobarbitone. As the baby continued to be oxygen dependent, 2D Echocardiogram was done on Day 4 of life which showed Situs Solitus, Atrioventricular, Ventricular- Arterial Concordance, Dilated Right Atrium and Right Ventricles chamber, Pulmonary Artery Systolic Pressure of 45 mm Hg with no obvious VSD/ PDA/ PS/ COA. Colour turbulence was seen across IAS. The valves were normal, Reduced RV function, Normal LV function and No vegetation/ Pericardial effusion/ Clots were seen in the 2D Echo.

The baby was started on Tab. Sildenafil 1 mg /kg/dose every 6th hour and improved after 4 days. The baby was maintaining saturation at room air & there was no tachypnea. Hence, DBF was established, and the baby was discharged from NICU.

Case-2:

This term female 2.72 kg baby was born via Normal Vaginal delivery with meconium-stained amniotic fluid presented at birth with complaints of chest indrawing, decreased activity and bluish discoloration of lips.

The baby was admitted to NICU. On admission, the baby had a Heart Rate of 116 bpm, BP of 76/52mmHg (56), saturation of 70%. The baby was connected to CPAP with a setting of FiO2 of 60% and PEEP 5.

2D echocardiography was done which revealed Congenital Heart Disease, Large ASD 4-5 mm Left to Right shunt, Dilated RA, RV, Mild TR with moderate PAH, PASP=55 mmHg

However, baby had weak pulses and desaturation with CPAP. ABG done revealed High Anion Gap Metabolic Acidosis with Respiratory Alkalosis, Sodium Bicarbonate correction given.

The baby was connected to Mechanical Ventilator and started on Ionotropes and was started on Sildenafil at 1mg/kg/dose every 6th hour and IV antibiotics. The baby improved after 48 hours and was extubated and improved further after 6 days. The baby was maintaining saturation at room air and there was no tachypnea. Hence DBF was established, and the baby was discharged from NICU.

Case-3:

A Late Pre-Term baby (36weeks) male baby born via LSCS indicated for Meconium Stained Amniotic Fluid with a birth weight of 2.365 kg. On admission, the baby had a SARS score of 4/10. The baby was connected to CPAP with a FiO2 40% and PEEP 5 and was disconnected from CPAP after 3 days and switched over to Oxygen via nasal prongs. The baby was oxygen dependent hence 2D echo was done. 2D echocardiogram was done which showed Situs Solitus, Atrioventricular, Ventricular- Arterial Concordance, Dilated Right Atrium and Right Ventricles chamber, Pulmonary Artery Systolic Pressure of 45 mm Hg, No obvious VSD/ PDA/ PS/ COA, Colour turbulence seen across IAS, Normal valves, Reduced RV function, Normal LV function and No vegetation/ Pericardial effusion/ Clots.

The baby was started on Tab. Sildenafil at 1 mg/kg/dose every 6th hour. The baby improved on Day 7 and was no more oxygen dependent. Hence shifted out of NICU after DBF was established.

Case-4:

This Term female baby born via Emergency LSCS indicated for Fetal Bradycardia with birth weight of 2kgs with meconium-stained amniotic fluid. The baby cried after Bag and Mask ventilation and was admitted to NICU and connected with oxygen via prongs in view of Downes Score being 3/10. Prophylactic IV antibiotics was started. However, the baby had a room air saturation of 86% and was oxygen dependent.

On day 4 of life, 2D Echocardiography was done which showed Congenital Heart Disease, 4mm ostium secundum ASD with left to right shunt, Mildly dilated RA and RV and Mild TR with gradient 30mm Hg. The baby was started on Tab. Sildenafil 1mg /kg/dose every 6th hour and improved after 5 days. The baby was maintaining saturation at room air and there was no tachypnea. Hence, DBF was established, and the baby was discharged from NICU.

Case-5:

This 2.6 kg female term baby who is born via Caesarean Section in view of thick Meconium-Stained amniotic fluid was admitted to NICU at birth. The baby had a respiratory rate of 70 cycles per minute(tachypnea), heart rate of 152 beats per minute, Room air saturation of 40%, peripheral cyanosis and had Intercostal and Subcostal retraction. The baby was connected to CPAP with a flow of 6 litres/min, PEEP-4 and

FiO2 80%. The Chest X ray was suggestive of Bilateral Pneumothorax. Intercostal Drainage (ICD) was inserted, and baby was connected to mechanical ventilator after which started on Fentanyl Infusion.

2D echocardiogram was done which showed Situs Solitus, Atrioventricular, Ventricular- Arterial Concordance, Dilated Right Atrium and Right Ventricles chamber, Pulmonary Artery Systolic Pressure of 45 mm Hg. No obvious VSD/ PDA/ PS/ COA, Colour turbulence seen across IAS, Normal valves, Reduced RV function, Normal LV function and No vegetation/ Pericardial effusion/ Clots.

HRCT was done which showed Moderate Left Pneumothorax with Mild Pneumothorax with few cystic leucencies indicating Bilateral Lung Parenchymal Congestive Changes. The baby was started on Tab. Sildenafil at 1mg per kg per dose every 8th hour. For emergency vascular access Umbilical Venous Catheter was inserted. At 20 hours of life baby had bradycardia and started on Ionotropes. However, baby arrested at 22 hours of life.

III. Discussion

PPHN is frequently associated with underlying parenchymal lung disease or systemic illness, so that the therapy needs to focus on the underlying disease such as by using antibiotics for sepsis and other supportive management. Respiratory support which recruits the lungs and provides appropriate inflation to reduce pulmonary vascular resistance (PVR) is an important step in management of these newborns which lowers the risk of PPHN[8].

Our case series reported 5 babies with Persistent Pulmonary Hypertension of the newborn (PPHN) diagnosed with the help of 2D Echocardiography and they were managed in our hospital.

In our study, 4 babies were females (80%), and the other one was a male baby (20%) thereby showing a 4:1 female preponderance when compared with the males. However, in contrary to our report, studies done by Harish S et al, Choudhary et al and Hsieh et al showed a male preponderance of 62.9%, 63% and 62.5% respectively[12-14].

Our group had a high LSCS delivery rate, where only 2 babies were delivered through normal vaginal delivery and the remaining 3 babies were delivered through caesarean section (60%), which may have contributed to the development of PPHN by interfering with endogenous catecholamine secretion and delaying the changeover[12,13,15].

While PPHN is often more common in late preterm newborns (as reported by Steurer et al.)[16], only one baby (20%) born late preterm had this condition and more term infants (80%) were diagnosed with PPHN in the current study. Gustav et al.[17] and Harish S et al.[12] reported similar results, with 82.6% and 82.3% of term newborns compared to 20% preterm in their studies.

Echocardiography is the gold standard for confirming the diagnosis of PPHN, monitoring the effectiveness of therapeutic measures, and ruling out cyanotic or serious CHD[20,21]. All the 5 babies in our study underwent Echocardiography, where 2 of them were diagnosed to have Congenital heart diseases – Atrial Septal Defect (ASD).

PPHN continues to be one of the main causes of critical illness in the newborn intensive care unit (NICU), and mortality has remained unchanged at 5–10%[19]. In our study, the total PPHN mortality rate was 20%. A 26.7% mortality was observed by Hsieh et al.[14] 42.3% mortality by Harish S et al.[12] and 11% by Sukys et al.[6] This may be because the babies were only able to be treated with Oral Sildenafil at 1mg/kg/dose and conventional ventilation, whereas they were unable to be treated with iNO, HFOV, or ECMO.

The mechanism by which Sildenafil works is by the inhibition of phosphodiesterase type 5 (PDE 5), an enzyme that facilitates the breakdown of cGMP. Oral sildenafil (dose range: 1-2 mg/kg every 6 hours) improves oxygenation and lowers mortality which is a promising strategy in managing PPHN, according to studies[8,20]. Patients who have undergone prolonged hyperoxic ventilation, which enhances the formation of superoxide anions and boosts PDE5 activity, may benefit most from Sildenafil. The cornerstone of treatment for children with chronic pulmonary hypertension is oral sildenafil, which has been used in newborns with persistent pulmonary hypertension associated with BPD[20].

According to a study by Dinakara et al., Oral Sildenafil was well tolerated and showed improvement in infants with severe PPHN, indicating that it might be useful in the management of PPHN[22]. None of our babies experienced any side effects that were thought to be related to Sildenafil, and all of them responded well to the medication which was similar to the Pathak et al[11] study. In a retrospective analysis, Khorana et al.[23] found that at facilities without iNO and ECMO, Sildenafil might be a helpful adjuvant treatment for term newborns with pulmonary hypertension.

PPHN was primarily caused by MAS among 60% which was also an indication for LSCS in the present study. Similar results were obtained by Harish S et al.[12] Choudhary et al.[13] and Konduri et al.[18] in their respective studies.

4 babies improved between the 4th and 7th day of life except one baby led to death who had a bilateral pneumothorax who was diagnosed with Chest X-ray and HRCT.

IV. Conclusion

We conclude that, Persistent Pulmonary Hypertension of the newborn is a medical emergency seen in the neonates, which occurs due to failure of normal postnatal transition of fetal circulation. It's associated with high mortality and morbidity. Therefore, timely awareness regarding the predisposing conditions and early diagnosis and management may help to improve the outcome. Timely diagnosis and treatment of PPHN can reduce the morbidity and mortality. Sildenafil (1-3mg/kg every 6th hour) is shown to improve oxygenation and reduce mortality. Long term follow up is essential for these infants due to high risk of neurodevelopmental and hearing abnormalities.

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