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CASE REPORT

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Non cardiac central cyanosis in the newborn: A case report of persistent pulmonary hypertension of newborn (PPHN) and review of literature

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Abstract: PPHN is a fatal neonatal emergency resulting from poor respiratory transition to extra uterine life, in spite of several advances in the management thereof.

It is an uncommon disorder characterized by persistence of fetal circulation seen in about 1 - 5 per 1000 live birth. Advances in the management includes, inhaled nitric oxide (iNO) and extra corporeal membrane oxygenation (ECMO) as gold standard. However a third of patients will not respond to standard treatment, coupled with its dearth in some developing countries as Nigeria.

In recent studies, treatment with oral Sildenafil; a phosphodiesterase inhibitor type 5 (PDE5) showed reduction in pulmonary vascular resistance. This results in significant increase in oxygenation and a reduction in mortality without adverse effects. We report this uncommon case of one mo. old boy with PPHN who was seen in April 2019 at University of Nigeria Teaching Hospital Enugu. His clinical presentation, CXR and 2D Echo finding confirmed the diagnosis of PPHN. He was successfully managed with oral Sildenafil and Oxygen therapy. We recommend Sildenafil may be used as first-line treatment in settings where iNO, High Frequency Ventilation (HFV), and ECMO are unavailable.

Key words: Pulmonary hypertension, Newborn, Sildenafil.

Introduction

Persistent pulmonary hypertension of the newborn (PPHN) is a rare disorder of neonates.[1 - 4]

An elevated pulmonary vascular resistance is required for an effective fetal circulation; however, if this persists after birth, pulmonary to systemic shunting occurs through persisting fetal channels (e.g. ductus arteriosus), thereby blood bypasses the lungs resulting in systemic arterial hypoxaemia. [3, 4] We present a case of this rare disorder in Enugu that was managed successfully with oral Sildenafil. There is no reported case in literature of PPHN in our environment

Case Report

He is CC, a 1 mo old male child who presented in April 18th 2019, with fast breathing and bluish discoloration that was noted few days after birth. The bluish discoloration is present all the time.

There is no known exposure to radiation, alcohol, indomethacin, aspirin or selective serotinine reuptake inhibitors (SSRIs) in utero. These drugs are implicated in pulmonary vasoconstriction. Labour was at term lasted for 6 hours and child did not cry immediately after birth. He is the 4th in a monogamous nonconsangious marriage with four children two girls and 2♀& 2♂. Mother is 40 years while the father is 42years. There is no family history of cardiac defect or adverse cardiovascular event.

On examination: He was acutely ill looking. He had central cyanosis SaO_2 of 87% in room air. He was anicteric and a normal temp. 37.0°c Anthropometry were normal for age; with weight of 4.5kg, length of 57 cm.

He had Respiratory rate of 60bpm, Pulse rate of 140bpm. Apex beat was displaced to the 5th LICS AAL, HS = S1 + S2 with loud P2 and splitting of S2. Non tender hepatomegaly. Normal tone and reflexes in all the limbs. CXR showed cardiomegaly. (Figure 1) 2D Echo showed RVH with RV dominance, mild tricuspid regurgitation (TR) with a shunting patent foramen ovale (PFO), with no other cardiac shunt. (Figure 2)

A diagnosis of PPHN was made and he was started INO therapy at 5ml/l, Tab Sildenafil 10mg tids, Tab frusemide 5mg bd, Tab Enalapril 0.625mg daily for 2weeks. He made marked improvement, as saturation improved to 97% in room air and establishment of normal respiration. He was on follow up at the Cardiology clinic for 3 months, with no adverse event or return of symptoms and was discharged

Fig 1: CXR: Showing cardiomegaly with hyperinflation

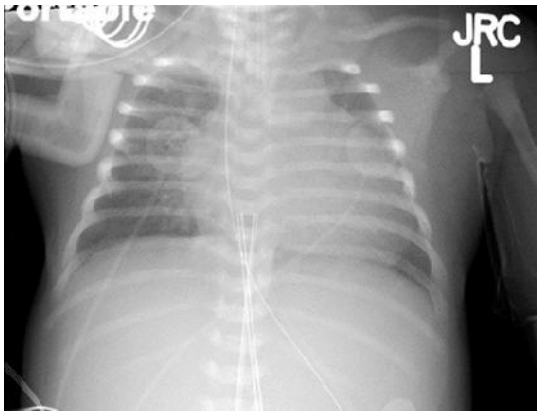
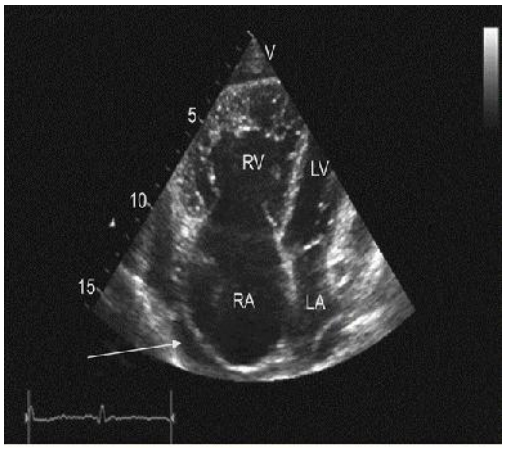


Fig 2: 2D Echo showed RVH with RV dominance and Moderate TR with RVSP = 45mmHg + RAP.
Moderate PAP = 55mmHg, Shunting PFO and mild pericardial effusion



Discussion

Persistent pulmonary hypertension of the newborn (PPHN) is a rare disorder of neonates. It is the persistent of fetal circulation and occurs in 1:1500 live births worldwide. Authors are not aware of any reported case of PPHN in our study environment.
An elevated pulmonary vascular resistance is required for an effective fetal circulation; however, if this persists after birth, pulmonary to systemic shunting occurs through persisting fetal channels (e.g. ductus arteriosus), thereby blood bypasses the lungs and resulting in systemic arterial hypoxaemia.[4, 5] This is shown in figure 1 and 2 as hyperinflation with cardiomegaly and RV dominance with mild TR.

In utero pathophysiologically, increased pulmonary resistance is maintained by fluid-filled lungs, decreased nitric oxide (NO) and prostacyclin (PGI2), and increased endothelin-1 (ET-1), And also products of the prostaglandin pathway, such as thromboxane and Serotonin [3, 6 -8]

PPHN is a transient event, which can be fatal without intensive and delicate neonatal management, to balanced ventilatory support and maintain low PCO_2, high PO_2 and pulmonary vasodilation. [3-5] The aim of treatment is selective pulmonary vasodilatation and the following methods are used based on the context of feasibility.
Ventilation strategies using ECMO & High-frequency oscillatory ventilation (HFOV)
or use of pulmonary vasodilators such as Magnesium sulfate, Sildenafil, Bosentan, and Inhaled nitric oxide (iNO).[5, 6, 8] Although iNO and ECMO are the gold standards [8, 9] they are expensive modalities associated with technical difficulties in developing countries.[4,5] Also up to 50-60% of newborn fail to respond to it. Hence there is need for effective therapies, to stabilize this newborn in our environment.

PPHN first reported in 1969 by Gersony et al. [1, 2] as persistence of fetal circulation in the absence of disease of the heart. Recently, sildenafil have helped shorten the course of this disease and reduce the mortality in these patients. [5, 7, 9]
The optimal dose of oral Sildenafil in children is a range of 0.5 - 2mg/kg/dose every 6 hours. [5, 7] Dosing is more frequent due to its short half-life. The patient received 1mg/kg 6 hourly with resolution of symptoms. Clinical indicators of a successful response were improved oxygenation indices with normalization in SaO_2 and stable vital signs.

The onset of action of Sildenafil varies from 20 minutes to 3 hours after oral administration. The concensus on duration of treatment is not well defined. The favored approach is to observe the individual response and stop medication after a clear response and to stop treatment after 6 - 8 doses without response.[5, 7, 9]
Dosage reduction or cessation of treatment is advised following side effects eg hypotension. Other side effect of Sildenfil includes retinopathy of prematurity. [5, 7, 9] An animal study showed that with improvement of pulmonary vascular resistance (PVR), there is associated systemic vasodilatation and deterioration of oxygenation when Sildenafil was administered with iNO. [9] There is need for caution when both are concurrently used.

The differential of PPHN is Idiopathic pulmonary arterial Hypertension (IPAH).
This resolves later than PPHN. Alveolar Capillary Dysplasia with misalignment of pulmonary veins. (ACD-MPV) This is a rare uniformly fatal disorder of neonates, in which there is misalignment between the pulmonary capillaries. It is refractory to therapy. Others include primary isolated parenchymal lung disease; (Pneumonia, transient tachypnea of the newborn, respiratory distress syndrome) [3, 5, 7, 9] These are differentiated by clinical setting and chest radiography. 2D Echo confirms the diagnosis of PPHN.

We conclude that in PPHN, administration of Sildenafil was an effective treatment associated with an increase in the oxygenation and a reduction in mortality with no

side effects. We recommend Sildenafil as first-line treatment in settings where i NO and ECMO are unavailable.

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Authors' Contribution
Arodiwe IO initiated the case report, did the literature search and wrote the manuscript and with the other authors, Chinawa JN and Ujunwa FA did reviewed the manuscript for intellectual content and final approval of the version to be published.
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