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Case Report

Use of Oral Sildenafil in the Management of Persistent Pulmonary Hypertension of the Newborn: A Case Report and Review of Literature.

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Abstract

Persistent pulmonary hypertension of the newborn (PPHN) arises from failure of the normal circulatory transition that occurs postnatally and is characterised by increased pulmonary vascular resistance, leading to significant respiratory distress and hypoxaemia. Oral sildenafil administration is a potential alternative treatment for PPHN, especially when inhaled nitric oxide is unavailable.

A 72-hour-old term male neonate was referred on account of respiratory distress, and cyanosis was noticed at 30 minutes of life with RR of 76 bpm and SPO2 of 57% in room air. The baby was pale, cyanosed, icteric, and febrile (39.5°C). An initial assessment of Severe NNJ 2^0 to EONNS with background cyanotic congenital heart disease was made. An echocardiogram with colour Doppler interrogation confirmed the diagnosis of Persistent pulmonary hypertension of the newborn. The baby was commenced on compounded oral sildenafil @ 2mg/kg/dose 6 hourly in addition to oxygen therapy. Baby improved and was subsequently discharged home on oral sildenafil, which was discontinued after a normal repeat ECHO Scan done at 2 months of life. Oral compounded sildenafil was found to be a useful alternative in managing PPHN.

Keywords: Case Report, Cyanosis, Neonate, Nigeria, Persistent Pulmonary Hypertension of the Newborn, Resource-Limited Setting, Sildenafil.

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Introduction

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newborn is a critical condition characterised by the failure of the neonatal circulatory system to transition from fetal to extra-uterine life, leading to sustained elevated pulmonary vascular resistance. [1–4] This results in right-to-left shunting of blood, preventing adequate pulmonary blood flow and causing severe hypoxemia and respiratory distress. [2] PPHN is a significant contributor to neonatal morbidity and mortality, affecting approximately 1 in 2000 infants and posing substantial challenges in clinical management. [3,4] The pathophysiology involves both pulmonary vasoconstriction and vascular remodelling.[2,5]

The management of PPHN aims to reduce PVR and improve oxygenation, and the gold standard treatment in high-income countries is inhaled nitric oxide (iNO), a potent and selective pulmonary vasodilator. [2,6] However, a substantial proportion of infants with PPHN, up to 40%, may be resistant to iNO therapy or may not have access to it. [2,7,8] In such scenarios, alternative or adjuvant therapies are crucial. Oral sildenafil, a phosphodiesterase type 5 inhibitor, has emerged as a promising therapeutic option.[5,7,9,10] Sildenafil works by inhibiting PDE5, thereby reducing the degradation of cyclic guanosine monophosphate (cGMP) and amplifying nitric oxide-mediated vasodilation in the pulmonary vasculature. [5,9–11].

Studies from low-resource settings consistently report its adoption due to cost and availability, with positive outcomes in oxygenation and survival. [12–14] However, there is a notable scarcity of published data specifically from Nigeria on the use of sildenafil for PPHN. The available literature includes two case reports by Daniyan et al [15] in Ebonyi and Ogugua et al [16] in Enugu, documenting the successful management of Nigerian newborns with PPHN using compounded oral sildenafil, and highlighting its use as an alternative where inhaled nitric oxide is unavailable. The authors emphasised a "dearth of literature from Nigeria on PPHN and the use of compounded oral sildenafil," suggesting that while the practice exists, it is not yet widely reported or systematically studied.[15] This report, therefore, describes the successful use of oral sildenafil in managing a neonate with PPHN at the Benue State University Teaching Hospital, Makurdi, North Central Nigeria, and reviews the literature to highlight the evolving role of sildenafil in neonatal care.

Case Report

A 72-hour-old term male neonate was referred from a secondary facility in a nearby town, on account of respiratory distress. Symptom was noticed at 30minutes of life, and interventions such as intranasal oxygen, intravenous antibiotics (Ceftazidime and Gentamycin), and intravenous fluids were instituted prior to referral.

Baby was delivered at 38weeks' gestational age via an elective caesarean section on account of maternal short stature, short interpregnancy period and a previous scar. APGAR scores were 7 and 10 at the 1st and 5th minute, respectively. He cried spontaneously with a birthweight of 3.1kg.

Physical examination findings on admission showed a conscious neonate in obvious respiratory distress, evidenced by flaring of alar nasi, intercostal and subcostal recessions, pale, cyanosed, icteric, febrile (axillary temp: 39.5 $^{\circ}$C), not dehydrated, with no pedal oedema. Anthropometric measures were as follows: Weight was 2.5Kg (10th percentile for age and sex), Length was 50cm (50th percentile for age and sex) and Occipitofrontal circumference (OFC) was 35cm (between 50th and 85th percentile for age and sex).

Respiratory rate was 60 cpm, dyspneic with clear bronchovesicular breath sounds. Oxygen saturation (SPO_2) of 72%, 83% and 95% at room air, on intranasal oxygen and bubble Continuous Positive Airway Pressure (CPAP) @5L/m 5cmH_20, respectively, when recorded. The heart rate was 120 bpm, and the heart sounds were normal SI & SII, with no murmur. Other systemic examinations were essentially normal.

An initial assessment of Neonatal Jaundice secondary to? Early Onset Neonatal Sepsis R/O ABO Incompatibility in a child with? Cyanotic Congenital Heart Disease.

Baby was admitted into the Special Care Baby Unit, blood samples were collected and sent for urgent Serum bilirubin, Full Blood Count with Reticulocyte count, Serum electrolytes, Blood group (baby and Mother), Blood Culture, Grouping, and cross-matching. Chest X-ray (AP-view) was requested (Figure 1), and Echocardiography was kept in view for when the baby is stable.

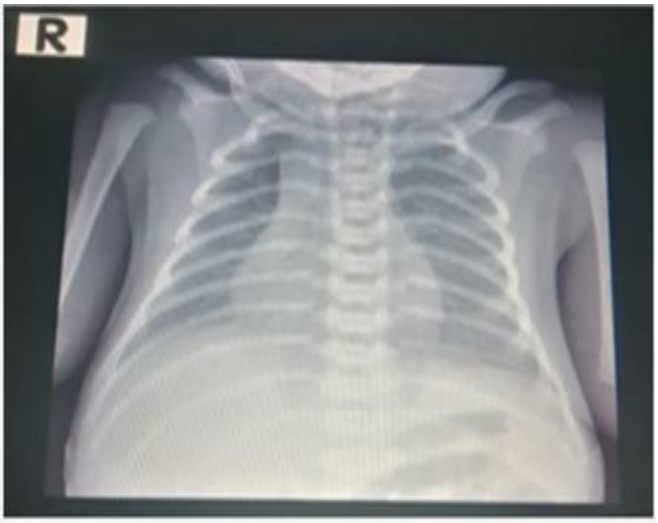

Figure 1: CXR at admission

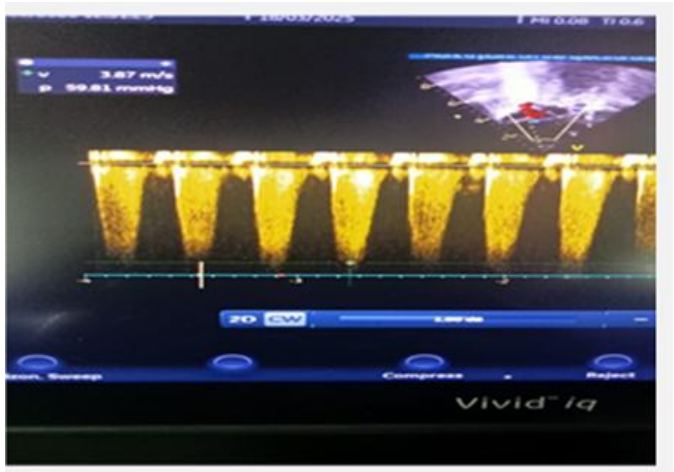

Figure 1: ECHO showing a continuous wave image of tricuspid regurgitation

The baby was placed on phototherapy, Bubble CPAP, intravenous Ciprofloxacin based on the unit protocol, and 8% Dextrose water in 1/5th saline while the clinical condition and vital signs were monitored closely. The results of the blood investigations showed unconjugated hyperbilirubinemia of 11.6mg/dL; blood culture was positive; and electrolytes, urea, and creatinine were normal.

Subsequent reviews on admission revealed a grade 2 systolic murmur and a loud P2. The initial diagnosis was sustained, and expressed breast milk (EBM) commenced while other medications were continued. Following further reviews, intravenous fluids were discontinued, EBM increased to 120ml/kg/d, and Echocardiography was requested.

The result of echocardiography on day 7 (Figure 2) showed a right-to-left shunt through an ostium secondum ASD on colour Doppler and a moderate tricuspid regurgitation with a velocity of 3.89 m/s and

peak gradient of 59.81mmhg on continuous wave interrogation, confirming the diagnosis of PPHN. The baby was commenced on suspension Sildenafil at 2mg/kg/dose 6-hourly, while antibiotics and feeding were continued. The baby showed marked clinical improvement from day 8 to 9, evidenced by resolution of cyanosis, tachypnea and tachycardia. Intranasal oxygen was discontinued on day 11, with SPO2 at 98% on room air. The baby was discharged on day 13 on suspension Sildenafil at 2mg/kg/dose 6-hourly.

Baby was seen in the outpatient clinic for follow-up a month later, and findings showed an adequately vaccinated male infant on exclusive breastfeeding, not cyanosed, weighing 3.6kg, and with stable vitals (RR-60 bpm, HR-140 Bpm, SPO_2-98%). A repeat echocardiography was requested, and the result showed a left-to-right shunt across an ostium secondum ASD, with resolved tricuspid regurgitation:

Discussion

The case highlights the use of oral sildenafil in the management of PPHN, particularly when conventional therapies are limited or unavailable. The observed improvement in the patient's condition aligns with the existing literature, suggesting that sildenafil has a role as a pulmonary vasodilator in neonates.[17,18] The diagnosis of PPHN is confirmed with Echocardiography [4,12,17] while other investigations such as arterial blood gases, chest X-ray and pulse oximetry are significant. In this case, the diagnosis was confirmed with echocardiography, but arterial blood gases could not be obtained.

Studies have shown that oral sildenafil can be an effective alternative when iNO is not available or when infants are iNO-resistant, facilitating weaning from iNO or serving as a primary treatment. [7–9,17] Oral sildenafil has been shown to significantly improve oxygenation and reduce pulmonary artery pressures in neonates with PPHN, especially where inhaled nitric oxide (iNO) is unavailable or unaffordable—a common scenario in Nigeria and similar settings.[12,13,17,20] In our context, iNO was not available, and hence the only available option was oral sildenafil, which was compounded and used as the primary treatment.

Studies report rapid decreases in right ventricular pressures, with most neonates showing clinical improvement within 24–48 hours of treatment. [12,18,19,21] The administration of sildenafil, often starting with a test dose of 0.5 mg/kg and gradually increasing to a maintenance dose, has been described in various contexts, with optimal dosing ranging between 0.5mg/kg and 2mg/kg.[9,17,22,23] Oral suspensions are available, making it feasible for neonatal populations.[24]. In this case, oral sildenafil was compounded by the hospital pharmacists and started at 2mg/kg/dose 6-hourly. The meta-analysis by Sun et al. [24] showed that doses of 1.5mg/kg were most effective in reducing pulmonary artery systolic pressure, while doses of 2mg/kg were most effective in increasing arterial oxygen saturation. The baby showed significant clinical improvement, evidenced by resolution of cyanosis, tachycardia, and tachypnea. The resolution of

symptoms that had persisted despite oxygen therapy and CPAP was noticed 48 hours after the commencement of sildenafil, and this was attributed to the effect of sildenafil, as a repeat ECHO showed a left-to-right shunt in contrast to the earlier right-to-left shunt following a fall in pulmonary artery pressure. This was in keeping with the reports of Monazea et al [17] and Kalimath et al [21], which also documented resolution of symptoms within 48 hours.

Multiple randomized controlled trials, meta-analyses, and systematic reviews consistently report that oral sildenafil is well tolerated in neonates with PPHN. Across studies, no significant short-term complications or clinically important side effects—such as systemic hypotension—have been observed when sildenafil is used as monotherapy at recommended doses. [13,14,21,25]

Rare side effects such as desaturations associated with airway spasm have been noted in some patient populations, particularly those with bronchopulmonary dysplasia or Trisomy 21. [25] Other reported side effects, like facial flushing, headaches, and nasal stuffiness, typically do not necessitate discontinuation of therapy.[25] However, the use of oral sildenafil in this baby was seen to have produced only clinical improvement without identifiable adverse effects during the course of administration.

Most studies have follow-up periods of only a few days to weeks, and further research is needed to assess potential long-term effects. [14,24] The baby was followed up for over eight months without any adverse effects reported.

The findings from this report, in conjunction with the reviewed literature, underscore the importance of oral sildenafil as a valuable therapeutic agent for PPHN. It offers a crucial option, especially in resource-limited settings, as in this case, where gold-standard therapies like iNO may not be accessible. [8]

Limitations

Arterial blood gas analysis was not performed, and iNO was unavailable.

Conclusion

Oral sildenafil is a valuable alternative for managing PPHN in Nigerian newborns, especially where standard therapy like iNO is inaccessible. This case report, when viewed alongside recent literature from Nigeria and beyond, supports the use of oral sildenafil as therapy for PPHN in resource-limited settings.

Recommendation

We recommend that health policymakers and hospital formularies in Nigeria consider the formal inclusion of oral sildenafil in national and institutional neonatal care protocols. Concurrently, efforts should be intensified to build capacity for diagnosing PPHN through training in functional echocardiography.

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