Oral Sildenafil as a Rescue Therapy in Presumed Acute Pulmonary Hypertensive Crisis

abstract

A 23-week-old baby, born at 26+2 weeks, presented to the hospital with critical respiratory failure, which was impossible to stabilize. She had unstable oxygen saturations between 35% and 95%. A presumptive diagnosis of bronchopulmonary dysplasia with associated pulmonary hypertensive crisis was made. In the absence of inhaled nitric oxide, 2 oral doses of 1 mg/kg sildenafil were given, with a dramatic improvement 30 to 45 minutes later. Her oxygenation index fell from 43 to 14. She made a full recovery and was discharged from the hospital 2 weeks later. Pediatrics 2013;131:e626–e628
Pulmonary hypertension occurs when there is an increase in pulmonary vascular pressure, which can then lead to a right to left shunt. Recognized treatment options include inhaled nitric oxide (NO), prostacyclin, and oral sildenafil, with supportive care as needed.\(^1\)\(^–\)\(^4\) Sildenafil has been used in pulmonary hypertension since 1999.\(^1\) It is becoming standard treatment of patients with chronic pulmonary hypertension and is also used as an emergency treatment of pulmonary hypertension of the newborn and newborn articles.\(^7\)\(^–\)\(^8\) We discuss a patient treated with sildenafil at a local hospital where inhaled NO was not available and rescue oral sildenafil was used to excellent effect.

**PATIENT**

The patient was born at 26\(^{+2}\) weeks by emergency caesarean delivery for severe maternal preeclampsia, with a birth weight of 599 g. She was ventilated for 31 days and then needed 11 days of noninvasive ventilation. She was diagnosed with chronic lung disease (CLD) and needed oxygen at discharge. Her other comorbidities included a patent ductus arteriosus and retinopathy of prematurity. She was discharged at 2 months’ corrected age with a weight of 3455 g, requiring 0.2 L of oxygen and nasogastric feed.

The patient presented to her local hospital the morning after discharge aged 23 weeks with a history of respiratory arrest. During an overnight feed, the baby stopped breathing and mother started cardiopulmonary resuscitation. On arrival to the emergency department, her heart rate was >100, but she was cold and blue with unrecordable oxygen saturations. Her initial capillary blood gas showed a pH of 6.99 with a pCO\(_2\) of 14.9 kPa. After limited improvement following a fluid bolus, antibiotics, and oxygen therapy, she was intubated and ventilated.

On arrival of the regional pediatric intensive care retrieval team, the saturations were 89% in 85% oxygen. After initial stabilization, difficulties were encountered in maintaining adequate oxygenation. Despite hand ventilating the patient in 100% oxygen, her oxygen saturations were fluctuating between 35% and 95%. Another chest radiograph ruled out a pneumothorax and showed severe CLD but no gross consolidation. The patient continued to deteriorate, and high pressures were needed to keep saturations >75% but were commonly in the 50s. Parents were advised that the baby was unlikely to survive the transfer.

In the absence of inhaled NO and faced with a severely sick patient with risk factors for pulmonary hypertension, a rescue dose of sildenafil 1 mg/kg was given via the nasogastric tube (Fig 1). Within 20 to 30 minutes a slight improvement was seen, but the saturations were still low, so an additional 1 mg/kg dose was given. Within 15 minutes, there was a marked improvement in the saturations, which remained >95% for the rest of the transfer. No side effects were observed; her blood pressure remained stable with her oxygenation index dropping from 43 to 14. On arrival to the regional pediatric ICU, the patient was started on high-frequency oscillation ventilation and inhaled NO. She made a good recovery and was transferred back to her local hospital within 2 weeks.

**DISCUSSION**

Sildenafil is a selective phosphodiesterase inhibitor and has been shown in studies to improve pulmonary hypertension in both adult and pediatric populations.\(^9\)\(^–\)\(^11\) The dosing regimen for acute pulmonary hypertension is not clear, and data are limited. One study demonstrated that plasma levels after doses of 0.5 to 2 mg/kg are similar to maximum plasma concentrations in adults on sildenafil.\(^12\) Potential reported side effects include arterial hypoxemia (due to increased intrapulmonary shunt) and hypotension.\(^1\)\(^,\)\(^2\)\(^,\)\(^7\)\(^,\)\(^13\)\(^,\)\(^14\) Sildenafil has been shown to have an onset of action in 30 to 120 minutes (mean 60 min)\(^10\) and has been shown to improve pulmonary arterial pressures, systemic saturations, and oxygen index and maintain V/Q matching.\(^5\)\(^–\)\(^10\)\(^,\)\(^11\) Theoretically, V/Q mismatching may occur due to global pulmonary vasodilatation, but no evidence of this was seen.

Pediatric intensive care teams undertaking transfers of critically ill children need to cope with critical situations in which advanced intensive care therapies are often not available.

![FIGURE 1](https://example.com/figure1.png)

**FIGURE 1**
Oxygen saturations over time: the first dose of sildenafil was given at 14:10.
Such teams need to make difficult choices as to the risks and benefits of novel treatments based on the patient’s pathophysiology.

Efficacy of this treatment is difficult to prove because we did not have pre- and posttreatment echocardiographic assessment of the pulmonary artery pressures. Although the improvement in the patient’s saturations might have been due to improved lung compliance, her ventilator pressure needs remained extremely high throughout the transfer period and beyond. The improvement was temporarily linked to the sildenafil dose with no other changes in management or physiologic parameters.

The successful outcome of this patient underlines the difficult scenarios undertaken by pediatric intensive care transfer teams. In this patient’s case, inaction would have probably led to the patient’s death. Transfer teams take risks on their patient’s behalf, making difficult decisions in the absence of a robust evidence base. For teams in such situations, it is important that their decisions are based on balancing the acute pathophysiology and the resources at hand and that they can be justified after the event.

CONCLUSION

Sildenafil is known to help in cases of chronic pulmonary hypertension, although evidence of its use in emergency situations is limited. We used a rescue dose of two 1 mg/kg doses of oral sildenafil in a case of presumed pulmonary hypertensive crisis. Our patient had a dramatic improvement in her ventilation and saturations within 45 minutes. We conclude that the use of sildenafil in the emergency treatment of presumed pulmonary hypertension was temporally associated with a life-saving clinical improvement with no evidence of side effects.

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